and fully homologous biologic Fc activity (complement and /or Fc receptor binding), and would likely result in less immunogenicity of the test article compared with AAB-001.
Scan Location: 3 Tesla MRI System, University of Oregon
Role: Board certified radiology Consultant

NIH GRANT: 2010-2012
Interictal Epileptiform Discharge (IED) Localization utilizing a volumetric (3D) brain imaging method which simultaneously provides both BOLD and cerebral perfusion information using a double spiral dual echo arterial spin labeling perfusion MRI (DSASL) technique. Study performed at both 3 and 4T.

PEER REVIEW PUBLICATIONS:

1. AJNR Am J Neuroradiol. 2011 Oct;32(9):1669-76. Epub 2011 Aug 18.

Impact of methodologic choice for automatic detection of different aspects of brain atrophy by using temporal lobe epilepsy as a model.

Scanlon C, Mueller SG, Tosun D, Cheong I, Garcia P, Barakos J, Weiner MW, Laxer KD.

Center for Imaging of Neurodegenerative Diseases and Department of Radiology, University of California-San Francisco, CA, USA.

BACKGROUND AND PURPOSE: VBM, DBM, and cortical thickness measurement techniques are commonly used automated methods to detect structural brain changes based on MR imaging. The goal of this study was to demonstrate the pathology detected by the 3 methods and to provide guidance as to which method to choose for specific research questions. This goal was accomplished by 1) identifying structural abnormalities associated with TLE with (TLE-mts) and without (TLE-no) hippocampal sclerosis, which are known to be associated with different types of brain atrophy, by using these 3 methods; and 2) determining the aspect of the disease pathology identified by each method.
MATERIALS AND METHODS: T1-weighted MR images were acquired for 15 TLE-mts patients, 14 TLE-no patients, and 33 controls on a high-field 4T scanner. Optimized VBM was carried out by using SPM software, DBM was performed by using a fluid-flow registration algorithm, and cortical thickness was analyzed by using FS-CT.
RESULTS: In TLE-mts, the most pronounced volume losses were identified in the ipsilateral hippocampus and mesial temporal region, bilateral thalamus, and cerebellum, by using SPM-VBM and DBM. In TLE-no, the most widespread changes were cortical and identified by using FS-CT, affecting the bilateral temporal lobes, insula, and frontal and occipital lobes. DBM revealed 2 clusters of reduced volume complementing FS-CT analysis. SPM-VBM did not show any significant volume losses in TLE-no.
CONCLUSIONS: These results demonstrate that the 3 methods detect different aspects of brain atrophy and that the choice of the method should be guided by the suspected pathology of the disease.

PMID: 21852375 [PubMed - in process]

2. Dis Aquat Organ. 2011 Sep 9;96(2):89-96.

Evidence of injury caused by gas bubbles in a live marine mammal: barotrauma in a California sea lion Zalophus californianus.

Van Bonn W, Montie E, Dennison S, Pussini N, Cook P, Greig D, Barakos J, Colegrove K, Gulland F.

Veterinary Science Department, The Marine Mammal Center, Sausalito, California 94965, USA. vanbonnb@tmmc.org

A yearling male California sea lion Zalophus californianus with hypermetric ataxia and bilateral negative menace reflexes was brought to The Marine Mammal Center, Sausalito, California, U.S.A., in late 2009 for medical assessment and treatment. The clinical signs were due to multiple gas bubbles within the cerebellum. These lesions were intraparenchymal, multifocal to coalescing, spherical to ovoid, and varied from 0.5 to 2.4 cm diameter. The gas composed 21.3% of the total cerebellum volume. Three rib fractures were also noted during diagnostic evaluation and were presumed to be associated with the gas bubbles in the brain. The progression of clinical signs and lesion appearance were monitored with magnetic resonance imaging, cognitive function testing and computed tomography. Gas filled voids in the cerebellum were filled with fluid on follow up images. Clinical signs resolved and the sea lion was released with a satellite tag attached. Post release the animal travelled approximately 75 km north and 80 km south of the release site and the tag recorded dives of over 150 m depth. The animal re-stranded 25 d following release and died of a subacute bronchopneumonia and pleuritis. This is the first instance of clinical injury due to gas bubble formation described in a living pinniped and the first sea lion with quantifiable cerebellar damage to take part in spatial learning and memory testing.

PMID: 22013748 [PubMed - indexed for MEDLINE]

3. Alzheimers Dement. 2011 Jul;7(4):396-401.

Prevalence of asymptomatic vasogenic edema in pretreatment Alzheimer's disease study cohorts from phase 3 trials of semagacestat and solanezumab.

Carlson C, Estergard W, Oh J, Suhy J, Jack CR Jr, Siemers E, Barakos J.

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BACKGROUND: Cerebral vasogenic edema (VE) has been reported to occur during antiamyloid immunotherapy. VE may be associated with central nervous system pathology with blood-brain barrier disruptions; however, less is known about the prevalence of naturally occurring VE in patients with Alzheimer's disease (AD). METHODS: Fluid-attenuated inversion recovery imaging sequences were obtained from four ongoing multicenter, randomized, double-blind, placebo-controlled, phase 3 trials in patients with mild-to-moderate AD. The first set of baseline scans was from patients in volumetric magnetic resonance imaging addenda in the Interrupting Alzheimer's Dementia by EvaluatiNg Treatment of Amyloid PaThologY (IDENTITY) studies examining semagacestat, a Î³-secretase inhibitor (cohort 1, n = 621). The second set of baseline scans was from the EXPanding alzhEimer's Disease InvestigaTIONs (EXPEDITION) studies examining solanezumab, an anti-AÎ² monoclonal

antibody (cohort 2, n = 2141). Readers were blinded to patient-identifying information and future treatment. A third set of baseline scans was from the first 700 patients who underwent protocol-specified magnetic resonance imaging before randomization in the EXPEDITION studies (cohort 3). The analysis used three neuroradiologists: two performed independent primary interpretations and the third was the adjudicator. Readers were blinded to patient information, treatment, protocol, and time point.
RESULTS: Four cases of asymptomatic VE were detected at baseline/screening. Two VE cases were due to underlying extra-axial mass lesions. The third VE case was associated with numerous microhemorrhages in keeping with cerebral amyloid angiopathy-related inflammation or AÎ²-related angiitis. The final VE case demonstrated localized sulcal fluid-attenuated inversion recovery imaging hyperintensity. No VE was detected in cohort 3 by readers blinded to patient baseline status.
CONCLUSIONS: VE seems to be rare at baseline in patients with AD in clinical trials, 2 of 2,762 associated with AD. Additional cohorts should be evaluated to support these findings.

PMID: 21784350 [PubMed - in process]

4. J Neurol. 2011 Apr;258(4):603-12. Epub 2010 Oct 26.

Widespread extrahippocampal NAA/(Cr+Cho) abnormalities in TLE with and without mesial temporal sclerosis.

Mueller SG, Ebel A, Barakos J, Scanlon C, Cheong I, Finlay D, Garcia P, Weiner MW, Laxer KD.

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MR spectroscopy has demonstrated extrahippocampal NAA/(Cr+Cho) reductions in medial temporal lobe epilepsy with (TLE-MTS) and without (TLE-no) mesial temporal sclerosis. Because of the limited brain coverage of those previous studies, it was, however, not possible to assess differences in the distribution and extent of these abnormalities between TLE-MTS and TLE-no. This study used a 3D whole brain echoplanar spectroscopic imaging (EPSI) sequence to address the following questions: (1) Do TLE-MTS and TLE-no differ regarding severity and distribution of extrahippocampal NAA/(Cr+Cho) reductions? (2) Do extrahippocampal NAA/(Cr+Cho) reductions provide additional information for focus lateralization? Forty-three subjects (12 TLE-MTS, 13 TLE-no, 18 controls) were studied with 3D EPSI. Statistical parametric mapping (SPM2) was used to identify regions of significantly decreased NAA/(Cr+Cho) in TLE groups and in individual patients. TLE-MTS and TLE-no had widespread extrahippocampal NAA/(Cr+Cho) reductions. NAA/(Cr+Cho) reductions had a bilateral fronto-temporal distribution in TLE-MTS and a more diffuse, less well defined distribution in TLE-no. Extrahippocampal NAA/(Cr+Cho) decreases in the single subject analysis showed a large inter-individual variability and did not provide additional focus lateralizing information. Extrahippocampal NAA/(Cr+Cho) reductions in TLE-MTS and TLE-no are

neither focal nor homogeneous. This reduces their value for focus lateralization and suggests a heterogeneous etiology of extrahippocampal spectroscopic metabolic abnormalities in TLE.

PMCID: PMC3065637
PMID: 20976465 [PubMed - indexed for MEDLINE]

5. Orbit. 2010 Dec;29(6):354-6.

Intra-lacrimal gland cavernous hemangioma.

Char DH, Barakos JA, Moretto J.

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Orbital cavernous hemangioma usually has a typical clinical and imagery pattern. We present a patient with an enlarged lacrimal gland due to an intra-gland cavernous hemangioma.

PMID: 21158578 [PubMed - indexed for MEDLINE]

6. Dis Aquat Organ. 2010 Sep 17;91(3):243-56.

Magnetic resonance imaging quality and volumes of brain structures from live and postmortem imaging of California sea lions with clinical signs of domoic acid toxicosis.

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Our goal in this study was to compare magnetic resonance images and volumes of brain structures obtained alive versus postmortem of California sea lions Zalophus californianus exhibiting clinical signs of domoic acid (DA) toxicosis and those exhibiting normal behavior. Proton density-(PD) and T2-weighted images of postmortem-intact brains, up to 48 h after death, provided similar quality to images acquired from live sea lions. Volumes of gray matter (GM) and white matter (WM) of the cerebral hemispheres were similar to volumes calculated from images acquired when the sea lions were alive. However, cerebrospinal fluid (CSF) volumes decreased due to leakage. Hippocampal volumes from postmortem-intact images were useful for diagnosing unilateral and bilateral atrophy, consequences of DA toxicosis. These volumes were similar to the volumes in the live sea lion studies, up to 48 h postmortem. Imaging formalin-fixed brains provided some information on brain structure; however, images of the hippocampus and surrounding structures were of poorer quality compared to the images acquired alive and postmortem-intact. Despite these issues, volumes of cerebral GM and WM, as well as the hippocampus, were similar to volumes calculated from images of live sea lions and sufficient to diagnose hippocampal atrophy. Thus, postmortem MRI scanning (either intact or formalin-fixed) with volumetric analysis can be used to investigate the acute, chronic and possible developmental effects of DA

on the brain of California sea lions.

PMID: 21133324 [PubMed - indexed for MEDLINE]

7. Epilepsia. 2010 Aug;51(8):1436-45. doi: 10.1111/j.1528-1167.2009.02413.x. Epub 2009 Dec 1.

Involvement of the thalamocortical network in TLE with and without mesiotemporal sclerosis.

Mueller SG, Laxer KD, Barakos J, Cheong I, Finlay D, Garcia P, Cardenas-Nicolson V, Weiner MW.

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PURPOSE: The thalamus plays an important role in seizure propagation in temporal lobe epilepsy (TLE). This study investigated how structural abnormalities in the focus, ipsilateral thalamus and extrafocal cortical structures relate to each other in TLE with mesiotemporal sclerosis (TLE-MTS) and without hippocampal sclerosis (TLE-no).
METHODS: Tâ, and high-resolution Tâ„ images were acquired on a 4T magnet in 29 controls, 15 TLE-MTS cases, and 14 TLE-no. Thalamus volumes were obtained by warping a labeled atlas onto each subject's brain. Deformation-based morphometry was used to identify regions of thalamic volume loss and FreeSurfer for cortical thickness measurements. CA1 volumes were obtained from high-resolution Tâ„ images. Multiple regression analysis and correlation analyses for voxel- and vertex-based analyses were performed in SPM2 and FreeSurfer.
RESULTS: TLE-MTS had bilateral volume loss in the anterior thalamus, which was correlated with CA1 volume and cortical thinning in the mesiotemporal lobe. TLE-no had less severe volume loss in the dorsal lateral nucleus, which was correlated with thinning in the mesiotemporal region but not with extratemporal thinning.
DISCUSSION: The findings suggest that seizure propagation from the presumed epileptogenic focus or regions close to it into the thalamus occurs in TLE-MTS and TLE-no and results in circumscribed neuronal loss in the thalamus. However, seizure spread beyond the thalamus seems not to be responsible for the extensive extratemporal cortical abnormalities in TLE.

PMCID: PMC2888933
PMID: 20002143 [PubMed - indexed for MEDLINE]

8. Orbit. 2010 Aug;29(4):216-8.

Fibrous dysplasia.

Char DH, Barakos JA, Cobbs CS, Shiel MJ.

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An atypical presentation of fibrous dysplasia with a very large cystic component is described. The MR pattern was not diagnostic.

PMID: 20812841 [PubMed - indexed for MEDLINE]

9. Lancet Neurol. 2010 Apr;9(4):363-72. Epub 2010 Feb 26.

11C-PiB PET assessment of change in fibrillar amyloid-beta load in patients with Alzheimer's disease treated with bapineuzumab: a phase 2, double-blind, placebo-controlled, ascending-dose study.

Rinne JO, Brooks DJ, Rossor MN, Fox NC, Bullock R, Klunk WE, Mathis CA, Blennow K, Barakos J, Okello AA, Rodriguez Martinez de Liano S, Liu E, Koller M, Gregg KM, Schenk D, Black R, Grundman M.

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Comment in
Lancet Neurol. 2010 Apr;9(4):333-5.

BACKGROUND: Carbon-11-labelled Pittsburgh compound B ((11)C-PiB) PET is a marker of cortical fibrillar amyloid-beta load in vivo. We used (11)C-PiB PET to investigate whether bapineuzumab, a humanised anti-amyloid-beta monoclonal antibody, would reduce cortical fibrillar amyloid-beta load in patients with Alzheimer's disease.
METHODS: Patients with mild-to-moderate Alzheimer's disease were randomly assigned to receive intravenous bapineuzumab or placebo in a ratio of seven to three in three ascending dose groups (0.5, 1.0, or 2.0 mg/kg). Each dose group was enrolled after safety review of the previous group. Randomisation was by interactive voice response system; masking was achieved with numbered kit allocation. Patients, investigators, study site personnel, sponsor staff, and carers were masked to treatment. Patients received up to six infusions, 13 weeks apart, and had (11)C-PiB PET scans at baseline and at weeks 20, 45, and 78. The primary outcome was the difference between the pooled bapineuzumab group and the pooled placebo group in mean change from screening to week 78 in (11)C-PiB cortical to cerebellar retention ratio averaged across six cortical regions of interest. Analysis was by modified intention to treat. This study is registered with EudraCT, number 2004-004120-12; ISRCTN17517446.
FINDINGS: 28 patients were assigned to bapineuzumab (n=20) or placebo (n=8). 19 patients in the bapineuzumab group and seven in the placebo group were included in the modified intention-to-treat analysis. Estimated mean (11)C-PiB retention ratio change from baseline to week 78 was -0.09 (95% CI -0.16 to -0.02; p=0.014) in the bapineuzumab group and 0.15 (95% CI 0.02 to 0.28; p=0.022) in the placebo group. Estimated mean difference in (11)C-PiB retention ratio change from baseline to week 78 between the bapineuzumab group and the placebo group was -0.24 (95% CI -0.39 to -0.09; p=0.003). Differences between the bapineuzumab group and the placebo group in the individual regions of interest were similar to the overall mean difference. Adverse events were typically mild to moderate in severity and transient. Two patients in the 2.0 mg/kg bapineuzumab group had transient cerebral vasogenic oedema.
INTERPRETATION: Treatment with bapineuzumab for 78 weeks reduced cortical

(11)C-PiB retention compared with both baseline and placebo. (11)C-PiB PET seems to be useful in assessing the effects of potential Alzheimer's disease treatments on cortical fibrillar amyloid-beta load in vivo.
FUNDING: Elan Pharmaceuticals and Wyeth Research.

PMID: 20189881 [PubMed - indexed for MEDLINE]

10. Alcohol Clin Exp Res. 2010 Jan;34(1):175-82. Epub 2009 Oct 23.

Age-related gray matter shrinkage in a treatment naÃ¯ve actively drinking alcohol-dependent sample.

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Background: We previously demonstrated, in a small sample, steeper age-related gray matter shrinkage in treatment naÃ¯ve alcohol-dependent (TxN) men compared to nonalcoholic controls, but could not separate out the contributions of age and lifetime duration of alcohol use (which were highly correlated) to this effect. In the current study, we have quadrupled the sample size and expanded it to include both men and women to try to replicate and extend the previous findings and to separate the contributions of age and alcohol use to the phenomenon. Methods: In the current study, we examine cortical gray matter volumes in 18- to 50-year-old TxN (n = 84) versus age and gender comparable controls (n = 67). We used a new Region of Interest Analysis method which accounts for differences in sulcal and gyral enfolding between individuals (Fein et al., 2009a). Results: We found greater age-related gray matter shrinkage in TxN than in controls. Partial correlation analysis showed that the effect was a function of age and not lifetime alcohol burden. Conclusions: Implications of the findings are discussed in terms of their contribution toward our knowledge of differences between different subpopulations of alcoholics and in terms of their implications for the morbidity of alcohol dependence in an aging national population.

PMCID: PMC2807906
PMID: 19860794 [PubMed - indexed for MEDLINE]

11. Neurology. 2009 Dec 15;73(24):2061-70. Epub 2009 Nov 18.

A phase 2 multiple ascending dose trial of bapineuzumab in mild to moderate Alzheimer disease.

Salloway S, Sperling R, Gilman S, Fox NC, Blennow K, Raskind M, Sabbagh M, Honig LS, Doody R, van Dyck CH, Mulnard R, Barakos J, Gregg KM, Liu E, Lieberburg I, Schenk D, Black R, Grundman M; Bapineuzumab 201 Clinical Trial Investigators.

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Comment in

Neurology. 2009 Dec 15;73(24):2052-3.
Neurology. 2010 Jun 15;74(24):2026; author reply 2026-7.

BACKGROUND: Bapineuzumab, a humanized anti-amyloid-beta (Abeta) monoclonal antibody for the potential treatment of Alzheimer disease (AD), was evaluated in a multiple ascending dose, safety, and efficacy study in mild to moderate AD.
METHODS: The study enrolled 234 patients, randomly assigned to IV bapineuzumab or placebo in 4 dose cohorts (0.15, 0.5, 1.0, or 2.0 mg/kg). Patients received 6 infusions, 13 weeks apart, with final assessments at week 78. The prespecified primary efficacy analysis in the modified intent-to-treat population assumed linear decline and compared treatment differences within dose cohorts on the Alzheimer's Disease Assessment Scale-Cognitive and Disability Assessment for Dementia. Exploratory analyses combined dose cohorts and did not assume a specific pattern of decline.
RESULTS: No significant differences were found in the primary efficacy analysis. Exploratory analyses showed potential treatment differences ($p < 0.05$, unadjusted for multiple comparisons) on cognitive and functional endpoints in study "completers" and APOE epsilon4 noncarriers. Reversible vasogenic edema, detected on brain MRI in 12/124 (9.7%) bapineuzumab-treated patients, was more frequent in higher dose groups and APOE epsilon4 carriers. Six vasogenic edema patients were asymptomatic; 6 experienced transient symptoms.
CONCLUSIONS: Primary efficacy outcomes in this phase 2 trial were not significant. Potential treatment differences in the exploratory analyses support further investigation of bapineuzumab in phase 3 with special attention to APOE epsilon4 carrier status. Classification of evidence: Due to varying doses and a lack of statistical precision, this Class II ascending dose trial provides insufficient evidence to support or refute a benefit of bapineuzumab.

PMCID: PMC2790221
PMID: 19923550 [PubMed - indexed for MEDLINE]

12. Alcohol Clin Exp Res. 2009 Oct;33(10):1806-14. Epub 2009 Jul 23.

Parietal gray matter volume loss is related to spatial processing deficits in long-term abstinent alcoholic men.

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BACKGROUND: We previously demonstrated relatively intact cognitive function (with the exception of suggestive evidence for persistent deficits in spatial information processing) in middle-aged long-term abstinent alcoholics (LTAA, abstinent for 6 months or more) compared to age and gender comparable nonalcoholic controls (NAC) (Fein et al., 2006).
METHODS: In the current study, we examine cortical gray matter volumes in the same samples to determine whether gray matter volumes in LTAA are consistent with the cognitive results--i.e., exhibiting gray matter volumes comparable to NAC in most brain regions, except for possible indications of persistent shrinkage in the parietal lobe subserving spatial information processing.
RESULTS: We found gray matter shrinkage in LTAA in the parietal lobe consistent with the spatial processing deficits in this same sample. More compelling, in

LTAA, the magnitude of parietal gray matter shrinkage was negatively associated with spatial processing domain performance and positively associated with alcohol dose. Gray matter volume deficits were present in the occipital and other cortical tissue, but poorer visuospatial test performance correlated significantly with smaller volumes in the parietal cortex only.
CONCLUSIONS: Taken together, the cognitive and structural imaging data provide compelling evidence that chronic alcohol abuse results in shrinkage of the parietal cortex with associated deficits in spatial information processing.

PMCID: PMC2755629
PMID: 19645730 [PubMed - indexed for MEDLINE]

13. Anat Rec (Hoboken). 2009 Oct;292(10):1523-47.

Neuroanatomy and volumes of brain structures of a live California sea lion (Zalophus californianus) from magnetic resonance images.

Montie EW, Pussini N, Schneider GE, Battey TW, Dennison S, Barakos J, Gulland F.

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The California sea lion (Zalophus californianus) has been a focal point for sensory, communication, cognition, and neurological disease studies in marine mammals. However, as a scientific community, we lack a noninvasive approach to investigate the anatomy and size of brain structures in this species and other free-ranging, live marine mammals. In this article, we provide the first anatomically labeled, magnetic resonance imaging-based atlas derived from a live marine mammal, the California sea lion. The brain of the California seal lion contained more secondary gyri and sulci than the brains of terrestrial carnivores. The olfactory bulb was present but small. The hippocampus of the California sea lion was found mostly in the ventral position with very little extension dorsally, quite unlike the canids and the mustelids, in which the hippocampus is present in the ventral position but extends dorsally above the thalamus. In contrast to the canids and the mustelids, the pineal gland of the California sea lion was strikingly large. In addition, we report three-dimensional reconstructions and volumes of cerebrospinal fluid, cerebral ventricles, total white matter (WM), total gray matter (GM), cerebral hemispheres (WM and GM), cerebellum and brainstem combined (WM and GM), and hippocampal structures all derived from magnetic resonance images. These measurements are the first to be determined for any pinniped species. In California sea lions, this approach can be used not only to relate cognitive and sensory capabilities to brain size but also to investigate the neurological effects of exposure to neurotoxins such as domoic acid.

PMID: 19768743 [PubMed - indexed for MEDLINE]

14. Epilepsia. 2009 Jun;50(6):1474-83. Epub 2009 Mar 12.

Subfield atrophy pattern in temporal lobe epilepsy with and without mesial sclerosis detected by high-resolution MRI at 4 Tesla: preliminary results.

Mueller SG, Laxer KD, Barakos J, Cheong I, Garcia P, Weiner MW.

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PURPOSE: High-resolution magnetic resonance imaging (MRI) at 4 Tesla depicts details of the internal structure of the hippocampus not visible at 1.5 Tesla, and so allows for in vivo parcellation of different hippocampal subfields. The aim of this study was to test if distinct subfield atrophy patterns can be detected in temporal lobe epilepsy (TLE) with mesial temporal sclerosis (TLE-MTS) and without (TLE-no) hippocampal sclerosis.
METHODS: High-resolution T(2)-weighted hippocampal images were acquired in 34 controls: 15 TLE-MTS and 18 TLE-no. Entorhinal cortex (ERC), subiculum (SUB), CA1, CA2, and CA3, and dentate (CA3&DG) volumes were determined using a manual parcellation scheme.
RESULTS: TLE-MTS had significantly smaller ipsilateral CA1, CA2, CA3&DG, and total hippocampal volume than controls or TLE-no. Mean ipsilateral CA1 and CA3&DG z-scores were significantly lower than ipsilateral CA2, ERC, and SUB z-scores. There were no significant differences between the various subfield or hippocampal z-scores on either the ipsi- or the contralateral side in TLE-no. Using a z-score <or=-2.0 to identify severe volume loss, the following atrophy patterns were found in TLE-MTS: CA1 atrophy, CA3&DG atrophy, CA1 and CA3&DG atrophy, and global hippocampal atrophy. Significant subfield atrophy was found in three TLE-no: contralateral SUB atrophy, bilateral CA3&DG atrophy, and ipsilateral ERC and SUB atrophy.
DISCUSSION: Using a manual parcellation scheme on 4 Tesla high-resolution MRI, we found the characteristic ipsilateral CA1 and CA3&DG atrophy described in TLE-MTS. Seventeen percent of the TLE-no had subfield atrophy despite normal total hippocampal volume. These findings indicate that high-resolution MRI and subfield volumetry provide superior information compared to standard hippocampal volumetry.

PMCID: PMC2804395
PMID: 19400880 [PubMed - indexed for MEDLINE]

15. Neuroimage. 2009 Jun;46(2):353-9. Epub 2009 Feb 26.

Widespread neocortical abnormalities in temporal lobe epilepsy with and without mesial sclerosis.

Mueller SG, Laxer KD, Barakos J, Cheong I, Garcia P, Weiner MW.

Center for Imaging of Neurodegenerative Diseases and Department of Radiology, University of California, San Francisco, CA 94121, USA. susanne.mueller@ucsf.edu

PURPOSE: Extrafocal structural abnormalities have been consistently described in temporal lobe epilepsy (TLE) with mesial temporal lobe sclerosis (TLE-MTS). In TLE without MTS (TLE-no) extrafocal abnormalities are more subtle and often require region of interest analyses for their detection. Cortical thickness measurements might be better suited to detect such subtle abnormalities than conventional whole brain volumetric techniques which are often negative in TLE-no. The aim of this study was to seek and characterize patterns of cortical

thinning in TLE-MTS and TLE-no.
METHODS: T1 weighted whole brain images were acquired on a 4 T magnet in 66 subjects (35 controls, 15 TLE-MTS, 16 TLE-no). Cortical thickness measurements were obtained using the FreeSurfer software routine. Group comparisons and correlation analyses were done using the statistical routine of FreeSurfer (FDR, p=0.05).
RESULTS: TLE-MTS and TLE-no showed both widespread temporal and extratemporal cortical thinning. In TLE-MTS, the inferior medial and posterior temporal regions were most prominently affected while lateral temporal and opercular regions were more affected in TLE-no. The correlation analysis showed a significant correlation between the ipsilateral hippocampal volume and regions of thinning in TLE-MTS and between inferior temporal cortical thickness and thinning in extratemporal cortical regions in TLE-no.
CONCLUSION: The pattern of thinning in TLE-no was different from the pattern in TLE-MTS. This finding suggests that different epileptogenic networks could be involved in TLE-MTS and TLE and further supports the hypothesis that TLE-MTS and TLE-no might represent two distinct TLE syndromes.

PMCID: PMC2799165
PMID: 19249372 [PubMed - indexed for MEDLINE]

16. Alcohol Clin Exp Res. 2009 Jan;33(1):70-8. Epub 2008 Oct 18.

Increased white matter signal hyperintensities in long-term abstinent alcoholics compared with nonalcoholic controls.

Fein G, Shimotsu R, Di Sclafani V, Barakos J, Harper C.

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BACKGROUND: The harmful effects of alcohol dependence on brain structure and function have been well documented, with many resolving with sufficient abstinence. White matter signal hyperintensities (WMSH) are thought to most likely be consequences secondary to the vascular (i.e., hypertension and atherosclerosis) effects of AD. We hypothesized that such effects would persist into long-term abstinence, and evaluated them in middle-aged long-term abstinent alcoholics (LTAA) compared with age and gender comparable nonalcoholic controls (NAC).
METHODS: Ninety-seven participants (51 LTAA and 46 NAC) underwent cognitive, psychiatric, and structural brain magnetic resonance image evaluations. WMSH were identified and labeled as deep or periventricular by an automated algorithm developed in-house. WMSH volumes were compared between groups, and the associations of WMSH measures with demographic, alcohol use, psychiatric, and cognitive measures were examined within group.
RESULTS: Long-term abstinent alcoholics had more WMSH than NAC. There was a significant group by age interaction, with WMSH increasing with age in LTAA, but not in NAC. Within LTAA, WMSH load was independently positively associated with alcohol burden and with age. No associations were evident between WMSH volumes and abstinence duration, family drinking history, years of education, or psychiatric or cognitive variables.
CONCLUSION: The magnitude of alcohol abuse was related to increased WMSH volume. The presence of an age effect in the LTAA but not the controls indicates a

synergistic effect wherein alcohol advances the onset of aging-related WMSH formation. The increased WMSH load did not appear to have any significant clinical correlates, indicating that the white matter lesions in our sample may not have been severe enough to manifest as cognitive deficits. A limitation of the study is that we did not have data on the presence or severity of lifetime or current indices of vascular risk factors such as hypertension, smoking, or diabetes.

PMCID: PMC2629790
PMID: 18976350 [PubMed - indexed for MEDLINE]

17. Proc Biol Sci. 2008 Feb 7;275(1632):267-76.

Novel symptomatology and changing epidemiology of domoic acid toxicosis in California sea lions (Zalophus californianus): an increasing risk to marine mammal health.

Goldstein T, Mazet JA, Zabka TS, Langlois G, Colegrove KM, Silver M, Bargu S, Van Dolah F, Leighfield T, Conrad PA, Barakos J, Williams DC, Dennison S, Haulena M, Gulland FM.

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Comment in
Epilepsy Curr. 2009 Sep-Oct;9(5):142-3.

Harmful algal blooms are increasing worldwide, including those of Pseudo-nitzschia spp. producing domoic acid off the California coast. This neurotoxin was first shown to cause mortality of marine mammals in 1998. A decade of monitoring California sea lion (Zalophus californianus) health since then has indicated that changes in the symptomatology and epidemiology of domoic acid toxicosis in this species are associated with the increase in toxigenic blooms. Two separate clinical syndromes now exist: acute domoic acid toxicosis as has been previously documented, and a second novel neurological syndrome characterized by epilepsy described here associated with chronic consequences of previous sub-lethal exposure to the toxin. This study indicates that domoic acid causes chronic damage to California sea lions and that these health effects are increasing.

PMCID: PMC2593718
PMID: 18006409 [PubMed - indexed for MEDLINE]

18. Orbit. 2007 Mar;26(1):75-7.

Cystic orbital metastasis from endometrial carcinoma.

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PURPOSE: To describe a rare orbital metastasis with atypical presentation.
DESIGN AND METHODS: Retrospective case report.
RESULTS: The patient presented with a rapid onset of a cystic orbital lesion after a presumptive diagnosis of endometrial carcinoma that had been completely excised eight months ago. This was the initial presentation of widespread metastasis.
CONCLUSIONS: Endometrial carcinomas can metastasize to the orbit and may have a very atypical presentation.

PMID: 17510879 [PubMed - indexed for MEDLINE]

19. Neuroimage. 2006 Sep;32(3):1465-71. Epub 2006 Jul 26.

Brain atrophy in long-term abstinent alcoholics who demonstrate impairment on a simulated gambling task.

Fein G, Landman B, Tran H, McGillivray S, Finn P, Barakos J, Moon K.

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We recently demonstrated impairment on the Simulated Gambling Task (SGT) in long-term abstinent alcoholics (AbsAlc). Brain regions that have been shown to be necessary for intact SGT performance are the ventromedial prefrontal cortex (VMPFC) and the amygdala; patients with VMPFC or amygdalar damage demonstrate SGT impairments similar to those of substance abusing populations. We examined these brain regions, using T1-weighted MRIs, in the 101 participants from our previous study using voxel-based morphometry (VBM). VBM was performed using a modification we developed [Fein, G., Landman, B., Tran, H., Barakos, J., Moon, K., Di Sclafani, V., Shumway, R., 2006. Statistical parametric mapping of brain morphology: sensitivity is dramatically increased by using brain-extracted images as inputs. Neuroimage] of Baron's procedure, [], in which we use skull-stripped images as input. We also restricted the analysis to a ROI consisting of the amygdala and VMPFC as defined by the Talairach Daemon resource. Compared to the controls, the AbsAlc participants had significant foci of reduced gray matter density within the amygdala. Thus, SGT decision-making deficits are associated with reduced gray matter in the amygdala, a brain region previously implicated in similar decision-making impairments in neurological samples. This structurally based abnormality may be the result of long-term alcohol abuse or dependence, or it may reflect a pre-existing factor that predisposes one to severe alcoholism. From an image analysis perspective, this work demonstrates the increased sensitivity that results from using skull-stripped inputs and from restricting the analysis to a ROI. Without both of these methodological advances, no statistically significant finding would have been forthcoming from this work.

PMCID: PMC1868686
PMID: 16872844 [PubMed - indexed for MEDLINE]

20. Neuroimage. 2006 May 1;30(4):1187-95. Epub 2006 Jan 25.

Statistical parametric mapping of brain morphology: sensitivity is dramatically increased by using brain-extracted images as inputs.

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A major attraction of voxel-based morphometry (VBM) is that it allows researchers to explore large datasets with minimal human intervention. However, the validity and sensitivity of the Statistical Parametric Mapping (SPM2) approach to VBM are the subject of considerable debate. We visually inspected the SPM2 gray matter segmentations for 101 research participants and found a gross inclusion of non-brain tissue surrounding the entire brain as gray matter in five subjects and focal areas bordering the brain in which non-brain tissue was classified as gray matter in many other subjects. We also found many areas in which the cortical gray matter was incorrectly excluded from the segmentation of the brain. The major source of these errors was the misregistration of individual brain images with the reference T1-weighted brain template. These errors could be eliminated if SPM2 operated on images from which non-brain tissues (scalp, skull, and meninges) are removed (brain-extracted images). We developed a modified SPM2 processing pipeline that used brain-extracted images as inputs to test this hypothesis. We describe the modifications to the SPM2 pipeline that allow analysis of brain-extracted inputs. Using brain-extracted inputs eliminated the non-brain matter inclusions and the cortical gray matter exclusions noted above, reducing the residual mean square errors (RMSEs, the error term of the SPM2 statistical analyses) by over 30%. We show how this reduction in the RMSEs profoundly affects power analyses. SPM2 analyses of brain-extracted images may require sample sizes only half as great as analyses of non-brain-extracted images.

PMCID: PMC1987363
PMID: 16442817 [PubMed - indexed for MEDLINE]

21. AJNR Am J Neuroradiol. 2006 Jan;27(1):9-10; author reply 10-1.

Presumed bilateral lateral geniculate nuclei ischemia.

Imes RK, Barakos J.

Comment on
AJNR Am J Neuroradiol. 2004 Oct;25(9):1544-8.

PMID: 16418347 [PubMed - indexed for MEDLINE]

22. J Neurol. 2005 Sep;252(9):1082-92. Epub 2005 Apr 29.

Metabolic characteristics of cortical malformations causing epilepsy.

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PURPOSE: Cortical malformations (CMs) are increasingly recognized as the epileptogenic substrate in patients with medically refractory neocortical epilepsy (NE). The aim of this study was to test the hypotheses that: 1. CMs are metabolically heterogeneous. 2. The structurally normal appearing perilesional zone is characterized by similar metabolic abnormalities as the CM.
METHODS: Magnetic resonance spectroscopic imaging (MRSI) in combination with tissue segmentation was performed on eight patients with NE and CMs and 19 age matched controls. In controls, NAA, Cr, Cho,NAA/Cr and NAA/Cho of all voxels of a given lobe were expressed as a function of white matter content and thresholds for pathological values determined by calculating the 95% prediction intervals. These thresholds were used to identify metabolically abnormal voxels within the CM and in the perilesional zone.
RESULTS: 30% of all voxels in the CMs were abnormal, most frequently because of decreases of NAA or increases of Cho. Abnormal voxels tended to form metabolically heterogeneous clusters interspersed in metabolically normal regions. Furthermore, 15% of all voxels in the perilesional zone were abnormal, the most frequent being decreases of NAA and Cr.
CONCLUSION: In CMs metabolically normal regions are interspersed with metabolically heterogeneous abnormal regions. Metabolic abnormalities in the perilesional zone share several characteristics of CMs and might therefore represent areas with microscopic malformations and/or intrinsic epileptogenicity.

PMCID: PMC2709485
PMID: 15868069 [PubMed - indexed for MEDLINE]

23. Epilepsia. 2004 Dec;45(12):1580-9.

Identification of the epileptogenic lobe in neocortical epilepsy with proton MR spectroscopic imaging.

Mueller SG, D Laxer K, Barakos JA, Cashdollar N, Flenniken DL, Vermathen P, Matson GB, Weiner MW.

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PURPOSE: The aim of this study was to evaluate the usefulness of multislice magnetic resonance spectroscopic imaging (MRSI) in combination with tissue segmentation for the identification of the epileptogenic focus in neocortical epilepsy (NE).
METHODS: Twenty patients with NE (10 with MRI-visible malformations, 10 with normal MRI) and 19 controls were studied. In controls, N-acetylaspartate NAA/Cr and NAA/Cho of all voxels of a given lobe were expressed as a function of white matter, and thresholds were determined by calculating the 95% prediction intervals (PIs) for NAA/Cr and NAA/Cho. Voxels with NAA/Cr or NAA/Cho values less than the 95% PI were defined as "pathological." Z-scores were calculated. Depending on the magnitude of those z-scores, we used two different methods (score-localization or forced-localization) to identify in a given subject the lobe with the highest percentage of pathological voxels, which was supposed to represent the epileptogenic lobe.
RESULTS: MRSI correctly identified the lobe containing the epileptogenic focus as

defined by EEG in 65% of the NE patients. MRSI localization of the focus was correct in 70% of the patients with an MRI-visible malformation and in 60% of the patients with normal MRI. Of the patients, 15% had metabolically abnormal brain regions outside the epileptogenic lobe, and 35% of the patients had evidence for secondary hippocampal damage.
CONCLUSIONS: MRSI may be helpful for the identification of the epileptogenic focus in NE patients, even in NE with normal MRI.

PMCID: PMC2744685
PMID: 15571516 [PubMed - indexed for MEDLINE]

24. Psychiatry Res. 2004 Jul 30;131(2):169-76.

Controlling for premorbid brain size in imaging studies: T1-derived cranium scaling factor vs. T2-derived intracranial vault volume.

Fein G, Di Sclafani V, Taylor C, Moon K, Barakos J, Tran H, Landman B, Shumway R.

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Intracranial vault (ICV) volume, obtained from T2-weighted magnetic resonance imaging (MRI), is generally used to estimate premorbid brain size in imaging studies. T1-weighted sequences lack the signal characteristics for ICV measurements [they have poor contrast at the outer boundary of sulcal cranium scaling factor (CSF)] but are valuable in imaging studies due to their excellent gray vs. white matter contrast. Smith et al. [NeuroImage 17 (2002) 479] suggested a T1-derived cranium scaling factor as an alternative control variable for premorbid brain size in cross-sectional studies. This index, which is computed using the SIENAX software, is a scaling factor comparing an individual's skull to a template skull derived from the Montreal Neurological Institute (MNI) average of 152 T1 studies (the MNI152). SIENAX computes coarsely defined estimates for the individual and MNI skulls rather than well-defined volumes. To test how well this approach would work as a control variable for premorbid brain size in cross-sectional studies, we compared the T1-derived cranium scaling factor to T2-derived ICV measurements in a sample of 92 individuals: 39 white males, 22 white females, and 31 African-American males, with an age range of 26-78 years. The correlation between T1- and T2-derived variables was 0.94 and did not differ across subject groups. The T1-derived cranium scaling factor accounted for a statistically significant portion (87%) of the variance of the T2-derived ICV measure and thus is a good surrogate for ICV measurement of premorbid brain size as a reference measure in MRI atrophy studies. Furthermore, neither race, sex, nor age accounted for any additional variance in ICV, indicating that neither race-, gender-, nor age-associated cranial bone thickness effects were present in this data set.

PMID: 15313523 [PubMed - indexed for MEDLINE]

25. J Vasc Interv Radiol. 2003 Oct;14(10):1329-32.

Ovarian protection by occlusion of uteroovarian collateral vessels before uterine fibroid embolization.

Marx M, Wack JP, Baker EL, Stevens SK, Barakos JA.

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In an attempt to decrease the incidence of premature ovarian failure, three patients with prominent ovarian collateral vessels from the uterine artery (UA) underwent collateral vessel embolization before uterine fibroid embolization. UA anatomy and collateral pathways are reviewed.

PMID: 14551281 [PubMed - indexed for MEDLINE]

26. J Vasc Interv Radiol. 2002 Dec;13(12):1282.

Re: Treatment of a splenic artery aneurysm with use of a stent-graft.

Marx M, Wack J, Baker E, Barakos J.

Comment on
J Vasc Interv Radiol. 2002 Jun;13(6):631-3.

PMID: 12471196 [PubMed - indexed for MEDLINE]

27. West J Med. 1999 Feb;170(2):112-5.

High-dose praziquantel with cimetidine for refractory neurocysticercosis: a case report with clinical and MRI follow-up.

Yee T, Barakos JA, Knight RT.

VA Palo Alto Health Care System, California, USA.

PMCID: PMC1305452
PMID: 10063399 [PubMed - indexed for MEDLINE]

28. J Vasc Interv Radiol. 1998 Sep-Oct;9(5):857-8.

Extravasation from power injection near previous arteriotomy site: a case for caution.

Marx M, Wack JP, Barakos JA, Andrews BT.

PMID: 9756085 [PubMed - indexed for MEDLINE]

29. Top Magn Reson Imaging. 1994 Summer;6(3):155-65.

Advances in magnetic resonance imaging of the head and neck.

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The head and neck encompass a tremendous spectrum of tissues in a compact space with almost every organ system represented, including the digestive and respiratory tracts, as well as the nervous, osseous, and vascular systems. Because of its anatomic complexity, this area tends to be approached with considerable trepidation. The high resolution of magnetic resonance imaging (MRI) and its outstanding definition of tissue contrast allow for an exquisite display of normal and pathologic anatomy. However, imaging of the head and neck, due to this intricate anatomy and the varied orientation of structures, demands much more attention to detail than do other areas of the body. This is underscored by the multitude of MRI sequences that can be employed. In this article I will review the application of various MRI techniques in the evaluation of the head and neck.

PMID: 7917319 [PubMed - indexed for MEDLINE]

30. Neurosurgery. 1992 Oct;31(4):621-7; discussion 627.

Magnetic resonance imaging of tuberculum sellae meningiomas: preventing preoperative misdiagnosis as pituitary macroadenoma.

Taylor SL, Barakos JA, Harsh GR 4th, Wilson CB.

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Despite recent advances in neurodiagnostic imaging, it may be difficult to differentiate tuberculum sellae meningiomas from pituitary macroadenomas preoperatively. Magnetic resonance (MR) imaging has supplanted computed tomography as the imaging modality of choice for sellar and parasellar lesions, but unenhanced MR imaging does not reliably distinguish between all tuberculum sellae meningiomas and pituitary macroadenomas. Accurate differentiation between these alternative diagnoses of a suprasellar mass is important because a tuberculum sellae meningioma always requires a craniotomy, whereas a transsphenoidal route is preferred for removing most pituitary macroadenomas. The gadolinium-enhanced MR images of seven patients with tuberculum sellae meningioma and seven with pituitary macroadenoma were reviewed retrospectively. Although no specific radiological feature was pathognomonic, a combination of several features allowed the correct diagnosis in all cases. Three characteristics of tuberculum sellae meningiomas distinguish them from pituitary macroadenomas: 1) bright homogeneous enhancement with gadolinium, as opposed to heterogeneous, relatively poor enhancement; 2) a suprasellar rather than a sellar epicenter of tumor; and 3) tapered extension of an intracranial dural base. Each of these findings can be subtle, but careful examination of gadolinium-enhanced, high-quality, thin section coronal and sagittal MR images of the parasellar region for this constellation of findings will allow the correct preoperative diagnosis in patients with either of these tumors.

PMID: 1407446 [PubMed - indexed for MEDLINE]

31. Radiology. 1992 Feb;182(2):573-5.

Lesions of the foramen ovale: CT-guided fine-needle aspiration.

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To verify perineural spread of tumor along the mandibular division of the trigeminal nerve in four patients, the authors obtained cytologic specimens by means of a CT-guided transfacial fine-needle aspiration technique. Diagnoses were squamous cell carcinoma (n = 3) and meningioma (n = 1). The technique allows biopsy of deep lesions that would otherwise require open surgical biopsy.

PMID: 1732985 [PubMed - indexed for MEDLINE]

32. Radiology. 1991 Sep;180(3):731-4.

Lateral tibial rim (Segond) fractures: MR imaging characteristics.

Weber WN, Neumann CH, Barakos JA, Petersen SA, Steinbach LS, Genant HK.

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The magnetic resonance (MR) imaging characteristics of lateral tibial rim (Segond) fractures and their associated injuries were reviewed in 12 patients with radiographic evidence of this fracture. Bone marrow adjacent to the fracture emitted a focally abnormal MR signal, which indicated an injury of the lateral capsular junction. The Segond fragment, however, was seen on MR images in only four of 12 patients. Associated ligamentous and meniscal injuries identified with MR imaging and arthroscopy involved the anterior (n = 11) and medial (n = 7) cruciate ligaments and the lateral (n = 4) and medial (n = 1) menisci. Focal bone marrow edema was due to injury of the lateral capsular junction. MR imaging evidence of such edema should indicate the presence of a lateral capsular injury and fracture, if one has not already been demonstrated with conventional radiography. A high association of Segond fractures with tears of the anterior cruciate ligament was confirmed, and MR imaging signs of a Segond fracture may therefore be used as indirect evidence for tears of that ligament.

PMID: 1871286 [PubMed - indexed for MEDLINE]

33. Radiology. 1991 Apr;179(1):191-8.

Orbit, skull base, and pharynx: contrast-enhanced fat suppression MR imaging.

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The high signal intensity of fat on T1-weighted magnetic resonance images has limited the utility of gadopentetate dimeglumine in imaging of the extracranial head and neck. Enhancing lesions may be obscured either by proximity to fat or by chemical misregistration artifact. The authors evaluated the role of a gadolinium-enhanced fat suppression imaging technique in the detection of extracranial head and neck abnormalities in 29 patients. These studies were directly compared with conventional pre- and postcontrast T1- and T2-weighted SE sequences. In detecting and defining the extent of abnormalities, fat-suppressed images were superior to non-fat-suppressed gadolinium-enhanced T1-weighted images in the majority of cases (22 of 27 [81%]). Fat-suppressed images were particularly beneficial in the detection of perineural spread of tumor as well as in defining lesions situated within or adjacent to fat-containing areas such as the base of the skull. These findings demonstrate that fat suppression techniques in combination with gadolinium enhancement are of value in extracranial head and neck imaging and should replace conventional postcontrast T1-weighted SE imaging.

PMID: 2006277 [PubMed - indexed for MEDLINE]

34. Curr Opin Radiol. 1991 Feb;3(1):93-100.

Imaging of the neck.

Barakos JA, Dillon WP.

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The neck encloses a tremendous spectrum of tissues in a compact space. The normal and pathologic anatomy of the neck can be exquisitely displayed with high-resolution CT and MR imaging. Accurate assessment of the neck requires a thorough knowledge of both its complex anatomy and the scope of pathologic entities that may affect the various cervical compartments. We review the advances in the past year that serve to improve our ability to identify and characterize pathology of the cervical soft tissues.

PMID: 2025514 [PubMed - indexed for MEDLINE]

35. AJNR Am J Neuroradiol. 1990 May;11(3):609.

Trigeminal sensory neuropathy caused by cervical disk herniation.

Barakos JA, D'Amour PG, Dillon WP, Newton TH.

University of California, San Francisco 94143-0628.

PMID: 2112329 [PubMed - indexed for MEDLINE]

36. Gastrointest Radiol. 1990 Spring;15(2):93-101.

Comparison of computed tomography and magnetic resonance imaging in the evaluation of focal hepatic lesions.

Barakos JA, Goldberg HI, Brown JJ, Gilbert TJ.

Department of Radiology, University of California, San Francisco 94131.

Two combined magnetic resonance (MR) spin-echo pulse sequences at 0.35 T were compared with dynamic bolus contrast-enhanced computed tomography (CT) in the evaluation of focal hepatic lesions. Each combined MR sequence was performed in a separate group of patients. The first group consisted of 76 patients in whom a moderately T1-weighted sequence (spin echo [SE] 500/30 [repetition time/echo time]) was combined with a T2-weighted sequence (SE 2000/60). In the second group, consisting of 68 patients, a more heavily T1-weighted sequence (SE 250/15) was combined with the T2-weighted sequence. All studies were evaluated in a retrospective blinded fashion, with construction of receiver operating characteristic curves. We conclude that, in detection of patients with one or more focal hepatic lesions, either combined MR sequence was comparable to CT. In the detection of individual hepatic lesions, the sensitivity of the combined MR sequence with a moderately T1-weighted sequence (SE 500/30 and 2000/60) was essentially equivalent to CT (79 vs 77%, respectively). Additionally, a combined MR sequence with a heavily T1-weighted pulse sequence (SE 250/15 and 2000/60) was not statistically different than CT (86 vs 80%, respectively). These findings were supported by the receiver operating characteristic analysis.

PMID: 2180780 [PubMed - indexed for MEDLINE]

37. J Comput Assist Tomogr. 1990 Jan-Feb;14(1):45-50.

MR imaging of acute transverse myelitis and AIDS myelopathy.

Barakos JA, Mark AS, Dillon WP, Norman D.

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Acute transverse myelitis (ATM) is a well recognized clinical entity, though its etiology remains obscure. Only a few reports of magnetic resonance imaging of ATM appear in the literature. These reports describe conflicting findings with respect to the signal intensity of the spinal cord on long repetition time (TR) sequences. The purpose of this study is to present our experience with five cases of ATM in which long TR sequences demonstrated abnormal increase in signal intensity of the cord. Magnetic resonance imaging also demonstrated extension of abnormal cord signal intensity over at least six spinal segments and above the clinically determined sensory level in four of five cases. Cord expansion was noted in two of five cases with normal myelograms. A case of acquired immunodeficiency syndrome (AIDS) myelopathy that demonstrated a similar high signal intensity of the cord is also presented. Our findings suggest that both ATM and AIDS myelopathy should be considered in the list of conditions that may result in a diffuse increase in the signal intensity of the cord on long TR sequences.

PMID: 2298996 [PubMed - indexed for MEDLINE]

38. J Comput Assist Tomogr. 1989 Sep-Oct;13(5):797-802.

High signal intensity lesions of the chest in MR imaging.

Barakos JA, Brown JJ, Brescia RJ, Higgins CB.

Department of Radiology, University of California School of Medicine, San Francisco.

The majority of pathologic lesions in the lung and mediastinum have relatively long T1 and T2 relaxation times and consequently yield medium to low signal intensity on T1-weighted images. Pulmonary lesions with high signal intensity on T1-weighted images are unusual and raise a special group of diagnostic considerations. In the current study, a mass with a lesion/fat signal intensity ratio of greater than 0.7 on a T1-weighted sequence was considered high signal intensity. The nature of these masses was ganglioneuroma or ganglioneuroblastoma (n = 3), atrial lipoma (lipomatous atrophy of the interatrial septum) (n = 3), pheochromocytoma (n = 2), bronchogenic cyst (n = 2), lymphangioma (n = 1), teratoma (n = 1), and a variety of primary and metastatic tumors of the mediastinum and lung. A single pathologic structure of these lesions was not present, but rather several underlying tissue compositions were noted, including fat, subacute hemorrhage, myxoid material, and cellular composition with high cytoplasmic/nuclear ratio. Thus, high signal intensity lesions of the thorax on T1-weighted images should suggest a number of differential diagnoses.

PMID: 2778135 [PubMed - indexed for MEDLINE]

39. AJR Am J Roentgenol. 1989 Jul;153(1):47-50.

MR imaging of secondary cardiac and paracardiac lesions.

Barakos JA, Brown JJ, Higgins CB.

Department of Radiology, University of California School of Medicine, San Francisco 94143.

PMID: 2735297 [PubMed - indexed for MEDLINE]

40. J Thorac Imaging. 1989 Apr;4(2):58-64.

Magnetic resonance imaging of cardiac and paracardiac masses.

Brown JJ, Barakos JA, Higgins CB.

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Magnetic resonance imaging (MRI) with ECG-gated acquisition displays the blood pool as a signal void and thereby provides high contrast differentiation between cardiovascular structures and soft-tissue masses. The role of MRI for the detection and definition of the extent of paracardiac and intracardiac masses is reviewed. The extension of mediastinal, lung, and upper abdominal tumors to the

heart and pericardium is depicted favorably by MRI and this attribute is also demonstrated. It is anticipated that MRI will have an increasing role in the evaluation of primary and secondary masses of the heart and pericardium.

PMID: 2716078 [PubMed - indexed for MEDLINE]

41. Clin Nucl Med. 1987 Nov;12(11):901-9.

Hepatobiliary scintigraphy and scintiangiography in abdominal trauma.

Colletti PM, Barakos JA, Ralls PW, Siegel ME, Halls JM.

University of Southern California School of Medicine, Los Angeles 90033.

Scintiangiography and hepatobiliary scintigraphy were performed in 45 patients with abdominal trauma. There were 18 gunshot wounds, six stab wounds, and 21 blunt injuries. Thirty-one of 45 patients showed abnormalities (69%). There were nine bilomas (4 with leaks), three leaks without biloma, (7 total leaks), five liver hematomas, three liver infarcts, one liver abscess, four renal injuries, one post-traumatic hepatic artery aneurysm, one acute acalculus cholecystitis, and four bowel injuries including one fistula, two obstructions, and one stricture. Two of the renal injuries and the hepatic artery aneurysm were identified only during scintiangiography. Eighteen of 38 gallbladders were not visualized despite normal bowel transit and delayed views to 4 hours (47%). Fourteen of 16 gallbladders were grossly normal at surgery, one had gallstones, and one had post-traumatic acalculus cholecystitis (6%). Hepatobiliary scintiangiography showed unique characteristics of vascular and renal lesions that were not seen on routine images. Sulfur colloid had no advantage over disofenin in evaluating liver injuries in nine cases. A high percentage of nonvisualized gallbladders (47%) were noted in acutely traumatized patients, and caution is recommended in diagnosing acute cholecystitis in the face of trauma.

PMID: 3427867 [PubMed - indexed for MEDLINE]

42. J Comput Assist Tomogr. 1987 Nov-Dec;11(6):1031-4.

Renal biopsy-related hemorrhage: frequency and comparison of CT and sonography.

Ralls PW, Barakos JA, Kaptein EM, Friedman PE, Fouladian G, Boswell WD, Halls J, Massry SG.

Department of Radiology, Los Angeles County/USC Medical Center.

To evaluate the frequency of retroperitoneal hemorrhage related to renal biopsy, we prospectively assessed 182 patients (200 biopsies) using state-of-the-art CT and ultrasound. Our study revealed definite CT evidence of hemorrhage after 90.9% of biopsies. In a blinded analysis of images obtained in biopsied patients and in unbiopsied control patients the overall accuracy of CT was 93.8 versus 76.4% for ultrasound. Our data suggest that detectable hemorrhage is virtually always seen after renal biopsy and its frequency is much higher than noted in earlier studies.

PMID: 3316324 [PubMed - indexed for MEDLINE]

43. Clin Nucl Med. 1987 Sep;12(9):744-50.

Kock continent ileal urinary reservoir. Anatomy and potential pitfalls of radionuclide imaging.

Barakos JA, Colletti PM, Siegel ME, Ralls PW, Halls JM.

Department of Radiology, University of Southern California School of Medicine, Los Angeles 90033.

The Kock continent ileal urinary reservoir (Kock pouch) is a new form of urinary diversion that, due to its advantages over previous techniques of urinary bypass, will probably become widespread in urologic practice. When bone imaging is performed in the presence of the Kock pouch, the unusual configuration of the pouch may obscure or simulate osseous lesions. An understanding of the surgical anatomy as well as the planar and SPECT scintigraphic appearances of the Kock pouch is necessary to avoid errors during interpretation. This series of 51 bone images reports on the variable scintigraphic appearance of the Kock pouch. In addition, the incidence and type of potentially avoidable pitfalls in the interpretation of bone imaging when this form of urinary diversion is used are evaluated.

PMID: 3499281 [PubMed - indexed for MEDLINE]

44. Clin Nucl Med. 1987 Jul;12(7):533-5.

Enterogastric reflux in suspected acute cholecystitis.

Colletti PM, Barakos JA, Siegel ME, Ralls PW, Halls JM.

Ninety patients undergoing Tc-99m disofenin hepatobiliary scintigraphy for suspected acute cholecystitis were assessed for enterogastric reflux. Seventy-seven cases showed bowel activity by one hour and were included in the study. Twenty-six percent (20/77) showed definite enterogastric reflux. The gastric activity tended to clear rapidly, even though patients remained supine during examination. Six of 20 patients (30%) with enterogastric reflux had gallbladder visualization. Of these six, one had acute cholecystitis and one had resolving acute cholecystitis with gallstone pancreatitis. There was one case each of pancreatitis, amebic abscess, sepsis, and one normal. Thus, of 20 patients with enterogastric reflux, 16 had acute cholecystitis (80%). Twenty-three of seventy-seven patients (30%) had surgically proven acute cholecystitis: of these, 16 of 23 (70% sensitivity) had gastric reflux, and 50 of 54 without acute cholecystitis did not have reflux (93% specificity). The overall accuracy of enterogastric reflux for acute cholecystitis is 86%. Gastric reflux seen on cholescintigraphy is a secondary sign of acute cholecystitis. Reflux may be related to duodenal irritation from the adjacent inflamed gallbladder.

PMID: 3608334 [PubMed - indexed for MEDLINE]

45. Radiology. 1987 Feb;162(2):415-8.

Cholelithiasis: evaluation with CT.

Barakos JA, Ralls PW, Lapin SA, Johnson MB, Radin DR, Colletti PM, Boswell WD Jr, Halls JM.

Computed tomography (CT) is often the first imaging modality used in the diagnosis of patients with suspected abdominal disease. While it is known that early generation CT scanners often detect gallstones, the detection rate of newer equipment is not widely known. Abdominal CT scans of 226 patients who had undergone ultrasonographic (US) studies of the gallbladder were reviewed in a blinded study to determine the accuracy of state-of-the-art CT scanning equipment in the detection of cholelithiasis. Of 110 patients with US or surgical evidence of cholelithiasis, gallstones were demonstrated on CT images of 87 (79.1% sensitivity). Overall accuracy was 89.8%, while specificity was 100%. On CT images stones could appear densely (48.3%) or slightly (11.5%) calcified, as an area with a rim of increased density (21.8%), as an area of soft-tissue density (14.9%), or as an area of low density (3.4%). Stone size, stone density, section incrementation, and the pericholecystic anatomy affected the detection rate. Understanding the spectrum of findings and the other factors involved can optimize success of diagnosis of cholelithiasis on the basis of CT examinations.

PMID: 3797654 [PubMed - indexed for MEDLINE]

46. Radiology. 1986 Nov;161(2):477-83.

Imaging of the Kock continent ileal urinary reservoir.

Ralls PW, Barakos JA, Skinner DG, Boswell WD Jr, Radin DR, Colletti PM, Halls JM.

The Kock continent ileal urinary reservoir (Kock pouch) is a new urinary bypass system that can overcome some of the principal complications associated with other forms of urinary diversion. It is important to understand the anatomy and radiology of this new technique since radiologists play an important role in evaluating the function of the Kock pouch as well as assessing its complications. The authors review the clinical and radiographic findings in 193 patients who had undergone Kock pouch urinary diversion. Patients are evaluated radiographically in the immediate postoperative period and at regular postoperative intervals for as long as 3 years. Routine evaluation consists of Kock pouch cystography followed by intravenous urography. When indicated, computed tomography, ultrasound, and interventional radiologic procedures are used. The normal anatomy as well as the radiographic appearance of the Kock pouch is presented. In addition, the radiographic appearance of pouch complications and their frequency are reviewed.

PMID: 3763919 [PubMed - indexed for MEDLINE]

47. J Urol. 1986 Sep;136(3):680-1.

Computerized tomography diagnosis of diffuse intraperitoneal metastases after retroperitoneal lymphadenectomy for testicular carcinoma.

Barakos JA, Jeffrey RB Jr, McAninch JW, Bottles K.

We report 2 cases of diffuse intraperitoneal metastases from testicular carcinoma following transabdominal retroperitoneal lymphadenectomy. This is an unusual pattern of metastasis for nonseminomatous germ cell tumors and it is believed to be the result of direct seeding from lymphatic leakage secondary to surgery. The value of computerized tomography in diagnosing this entity is emphasized.

PMID: 3735549 [PubMed - indexed for MEDLINE]

48. AJR Am J Roentgenol. 1986 Jun;146(6):1161-4.

CT in the management of periappendiceal abscess.

Barakos JA, Jeffrey RB Jr, Federle MP, Wing VW, Laing FC, Hightower DR.

Abdominal CT was the primary diagnostic method used to evaluate 40 patients with suspected periappendiceal abscess. Its subsequent impact on patient management was then analyzed for several categories of clinical presentation, including patients with and without a palpable right-lower-quadrant mass and postoperative patients. CT was reliable in distinguishing periappendiceal abscesses from phlegmons; 17 of 18 patients with phlegmons responded promptly to antibiotic therapy alone without need for surgery. Patients with larger, poorly localized abscesses underwent early surgical drainage. CT was successful in guiding percutaneous catheter drainage (nine patients) or aspiration (one patient) of well-localized periappendiceal abscesses in 10 of 11 patients. One attempted catheter drainage guided by sonography was technically unsuccessful. In patients without a palpable right-lower-quadrant mass, CT was helpful in establishing the diagnosis of periappendiceal inflammation. However, there were three false-positive diagnoses in patients with pericecal fluid collections including a ruptured cecal lymphoma, a ruptured cecal diverticulum, and a ruptured corpus luteum cyst. A diagnostic approach with CT is presented in patients with suspected periappendiceal abscess.

PMID: 3486560 [PubMed - indexed for MEDLINE]

49. The Lancet Neurology, Volume 11, Issue 3, Pages 241 - 249, March 2012
Amyloid-related imaging abnormalities in patients with Alzheimer's disease treated with bapineuzumab: a retrospective analysis
doi:10.1016/S1474-4422(12)70015-7
Published Online: 03 February 2012
Dr Reisa Sperling MD a , Prof Stephen Salloway MD b, Prof David J Brooks MD c, Donatella Tampieri MD d, Jerome Barakos MD e, Prof Nick C Fox MD f, Prof Murray Raskind MD g, Marwan Sabbagh MD h, Lawrence S Honig MD i, Prof Anton P Porsteinsson MD j, Ivan Lieberburg MD k, H Michael Arrighi PhD l, Kristen A Morris MS l, Yuan Lu MS l, Enchi Liu PhD l, Keith M Gregg PhD l, H Robert Brashear MD l, Gene G Kinney PhD l, Ronald Black MD m, Michael Grundman MD l n
a Center for Alzheimer Research and Treatment, Brigham and Women's Hospital, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
b Butler Hospital, Providence, RI, USA
c Centre for Neuroscience, Department of Medicine, Imperial College London, London, UK
d McGill University, Montreal, Canada

e California Pacific Medical Center, San Francisco, CA, USA
f UCL, Institute of Neurology, London, UK
g VA Medical Center, Seattle, WA, USA
h Cleo Roberts Center for Clinical Research/Sun Health Research Institute, Sun City, AZ, USA
i Columbia University, New York, NY, USA
j University of Rochester School of Medicine and Dentistry, Rochester, NY, USA
k Department of Internal Medicine, University of California, San Francisco, CA, USA
l Janssen Alzheimer Immunotherapy Research and Development, South San Francisco, CA, USA
m Pifzer, Collegeville, PA, USA
n Global R&D Partners, San Diego, CA, USA
Correspondence to: Dr Reisa Sperling, Harvard Medical School, Memory Disorders Unit, Brigham and Women's Hospital, Boston, MA 02115, USA
ARIA consist of a spectrum of imaging findings with variable clinical correlates, and some patients with ARIA-E remain asymptomatic even if treatment is continued. The increased risk of ARIA among APOE ε4 carriers, its association with high bapineuzumab dose, and its timecourse in relation to dosing suggest an association between ARIA and alterations in vascular amyloid burden.

50. MR imaging features of ARIA (amyloid-related imaging abnormalities) in patients treated with Bapineuzumab. Barakos, JA (Presentation).
12th International Stockholm/Springfield Symposium on Advances in Alzheimer Therapy

51. Prevalence of vasogenic edema and microhemorrhage in an Alzheimer's disease study population at baseline.
Christopher Carlson, Wahiba Estergard, Joonmi Oh, Joyce Suhy, Clifford Jack, Jerome Barakos, Eric Siemers
Presented:
Published: Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Vol. 7, Issue 4, S732
Published in issue: July, 2011

52. Vasogenic edema in the setting of ß-amyloid lowering therapy, adverse event: what is it and how is it detected?
Jerome Barakos, Christopher Carlson, Wahiba Estergard, Joonmi Oh, Joyce Suhy, Clifford Jack, Eric Siemers
Published: Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Vol. 7, Issue 4, e75
Published in issue: July, 2011

53. Prevalence of asymptomatic vasogenic edema in pretreatment Alzheimer's disease study cohorts from phase 3 trials of semagacestat and solanezumab
Christopher Carlson, Wahiba Estergard, Joonmi Oh, Joyce Suhy, Clifford R. Jack, Eric Siemers, Jerome Barakos
Published: Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Vol. 7, Issue 4, p396–401
Published in issue: July, 2011

54. Amyloid PET for Enrollment into AD Clinical Trials: Initial Experience and Potential Pitfalls (Presentation).
Jerome Barakos1,2, Derk Purcell1,2,3, Gregory Klein1, Joyce Suhy1, Joonmi Oh1, Ping Chiao4, Jeff Sevigny4
1Synarc Inc, Newark, CA, USA, 2California Pacific Medical Center, San Francisco, CA, USA, 3UC San Francisco, San Francisco, CA, USA, 4Biogen Idec, Cambridge, MA, USA
The 11th International Conference on Alzheimer's & Parkinson's Diseases
Florence, Italy, March 6-10, 2013

55. Amyloid PET Screening for Enrollment into AD Clinical Trials: Initial Experience in a Phase 1b Clinical Trial (Poster).

Jerome Barakos1,2, Derk Purcell1,2,3, Gregory Klein1, Joyce Suhy1, Joonmi Oh1, Ping Chiao4, Jeff Sevigny4
1Synarc Inc, Newark, CA, USA, 2California Pacific Medical Center, San Francisco, CA, USA, 3UC San Francisco, San Francisco, CA, USA, 4Biogen Idec, Cambridge, MA, USA
Alzheimer's Association 2013 International Conference (AAIC 2013)
International Event
Date(s): 07/13/2013 - 07/18/2013
Location: Boston Convention and Exhibition Center, 416 Summer Street, Boston, MA 02210

56. Amyloid PET Screening for Enrollment into AD Clinical Trials: An effective enrichment strategy in a Phase 1b Clinical Trial
Jerome Barakos[1,2], Derk Purcell[1,2,3], Gregory Klein[1], Joyce Suhy[1], Joonmi Oh[1], Ping Chiao[4], Jeff Sevigny[4]
Presented: CTAD Clinical Trials on Alzheimer's Disease - 6th Conference Alzheimer's Association International Conference (AAIC) in Copenhagen, Denmark (July 13-17, 2014).
Published: Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Vol. 9, Issue 4, P249
Published in issue: July, 2013

57. Amyloid PET screening results by APOE ε4 status from a Phase 1b clinical study 221AD103 in prodromal to mild AD patients
Authors: Chiao P, Suhy J, Barakos J, Burke M, Klein G, Verma A, Sevigny J
Presented: CTAD Clinical Trials on Alzheimer's Disease - 6th Conference Alzheimer's Association International Conference (AAIC) in Copenhagen, Denmark (July 13-17, 2014).
Published: Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Vol. 9, Issue 4, P291
Published in issue: July, 2013

58. Concordance of Quantitative SUVR Methods with Visual Assessment of Florbetapir PET Screening Results
Gregory Klein,1 Ping Chiao,2 Jerome Barakos,1,3 Derk Purcell,1,3,4 Mehul Sampat,1 Joonmi Oh,1 Jeff Sevigny,2 Joyce Suhy1
1Synarc Inc, Newark, CA, USA; 2Biogen Idec, Cambridge, MA, USA; 3California Pacific Medical Center, San Francisco, CA, USA; 4University of California San Francisco, San Francisco, CA, USA
Presented: Alzheimer's Association International Conference (AAIC) in Copenhagen, Denmark (July 13-17, 2014).
Published: Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Vol. 10, Issue 4, P399
Published in issue: July, 2014

59. Enrichment of early-stage AD patient recruitment to a Phase Ib study (221AD103) through amyloid PET screening by APOE ε4 status
Ping Chiao,1 Joyce Suhy,2 Jerome Barakos,2 Meredith Burke,2 Gregory Klein,2 Ajay Verma,1 Jeff Sevigny1
1Biogen Idec, Cambridge, MA, USA; 2Synarc, Inc, Newark, CA, USA
Presented: Alzheimer's Association International Conference (AAIC) in Copenhagen, Denmark (July 13-17, 2014).
Published: Alzheimer's & Dementia: The Journal of the Alzheimer's Association, Vol. 10, Issue 4, P263–P264
Published in issue: July, 2014

60. ARIA-E case descriptions from two placebo-controlled trials of solanezumab for the treatment of Alzheimer's disease.
Christopher Carlson, PhD1; Eric Siemers, MD1; Roza Hayduk2, Joyce Suhy, PhD3; Joonmi Oh, PhD 3; Jerome Barakos, MD3, 4
1Eli Lilly and Company or a wholly owned subsidiary, Indianapolis, IN, USA

2Quintiles, Indianapolis, IN, USA
3SynArc; Newark, CA, USA
4California Pacific Medical Center, San Francisco, CA, USA
Alzheimer's Association International Conference (AAIC) in Copenhagen, Denmark (July 13-17, 2014).

61. Amyloid-related imaging abnormities-hemosiderin (ARIA-H) in patients with Alzheimer's disease treated with bapineuzumab.
H. Michael Arrighi1, Jerome Barakos2, Fredrik Barkhof3, Clifford Jack Jr4, Donatella Tampieri5, Denis Melançon5, Kristen Morris6, Nzeera Ketter1, H. Robert Brashear1
1. Janssen Research & Development, South San Francisco, California, USA
2. California Pacific Medical Center, San Francisco, California, USA and Synac, Newark, California, USA
3. Image Analysis Centre, Department of Radiology VU University Medical Center, Amsterdam, The Netherlands; and Diagnostic Radiology, VU University Medical Center, Amsterdam, The Netherlands
4. Mayo Clinic, Rochester, Minnesota, USA
5. Neurology and Neurosurgery, McGill University, Montreal, Canada
6. Janssen Alzheimer Immunotherapy R&D, South San Francisco, CA, USA during the conduct of the study currently with BioMarin, San Rafael, CA USA

62. Amyloid PET imaging as a screening tool for enrollment into a Phase Ib clinical trial (221AD103) in patients with prodromal and mild Alzheimer's disease.
Jeff Sevigny, MD1, Joyce Suhy, PhD2, Ping Chiao, PhD1, Gregory Klein, PhD2, Joonmi Oh, PhD2, Derk Purcell, MD2,3,4, Ajay Verma, MD, PhD1, Mehul Sampat, PhD2,
Jerome Barakos, MD2,3 [Authors: Please check that we have your academic degrees correct]
(1) Biogen Idec, Cambridge, MA, USA
(2) Synarc Inc, Newark, CA, USA
(3) California Pacific Medical Center, San Francisco, CA, USA
(4) University of California San Francisco, San Francisco, CA, USA7th Clinical Trials on Alzheimer's Disease
Clinical Trials on Alzheimer's Disease - 7th Conference (CtaD) Philadelphia, November 20-22, 2014.

63. Enrichment of early-stage AD patient recruitment to a Phase Ib study (221AD103) through amyloid PET screening by APOE ε4 status.
Ping Chiao, PhD1, Joyce Suhy, PhD2, Jerome Barakos, MD2, Meredith Burke, PhD2, Gregory Klein, PhD2, Ajay Verma, MD, PhD1, Jeff Sevigny, MD1 [Authors: Please check that we have your academic degrees correct]
(1) Biogen Idec, Cambridge, MA, USA
(2) Synarc, Inc, Newark, CA, USA
Clinical Trials on Alzheimer's Disease - 7th Conference (CtaD) Philadelphia, November 20-22, 2014.
Presented: Thursday November 20, 2014

64. Amyloid-related imaging abnormities-hemosiderin (ARIA-H) in patients with Alzheimer's disease treated with bapineuzumab.
Authors:
H. Michael Arrighi, PhD1, Jerome Barakos, MD2, Fredrik Barkhof, MD, PhD3, Clifford Jack Jr, MD4, Donatella Tampieri, MD5, Denis Melançon, MD5, Kristen Morris, MS6, Nzeera Ketter, MD1, Enchi Liu, PhD1, H. Robert Brashear, MD1

(1) Janssen Research & Development, South San Francisco, California, USA
(2) California Pacific Medical Center, San Francisco, California, USA and Synac, Newark, California, USA
(3) Image Analysis Centre, Department of Radiology VU University Medical Center, Amsterdam, The

Netherlands; and Diagnostic Radiology, VU University Medical Center, Amsterdam, The Netherlands
(4) Mayo Clinic, Rochester, Minnesota, USA
(5) NeuroRx Research , Montreal, Canada
(6) Janssen Alzheimer Immunotherapy R&D, South San Francisco, CA, USA during the conduct of the study
CTAD (7th Clinical Trials Conference on Alzheimer's Disease) Philadelphia, Pennsylvania, USA from November 20 to 22, 2014.
Published: J Neurol Neurosurg Psychiatry doi:10.1136/jnnp-2014-309493

65. ARIA-E case descriptions from placebo-controlled and open-label trials of solanezumab for the treatment of Alzheimer's disease.
Christopher Carlson, PhD[1]; Eric Siemers, MD[1]; Roza Hayduk, MD[2], Joyce Suhy, PhD[3]; Joonmi Oh, PhD[3]; Jerome Barakos, MD[3, 4]
[1]Eli Lilly and Company or a wholly owned subsidiary, Indianapolis, IN, USA
[2]Quintiles, Indianapolis, IN, USA
[3]BioClinica; Newark, CA, USA
[4]California Pacific Medical Center, San Francisco, CA, USA
CTAD (7th Clinical Trials Conference on Alzheimer's Disease) Philadelphia, Pennsylvania, USA from November 20 to 22, 2014.

66. CONCORDANCE OF QUANTITATIVE SUVR METHODS WITH VISUAL ASSESSMENT OF FLORBETAPIR PET SCREENING RESULTS
Gregory Klein, Ping Chiao, Jerome Barakos, Derk Purcell, Mehul Sampat, Joonmi Oh, Jeff Sevigny, Joyce Suhy
Alzheimer's & Dementia: The Journal of the Alzheimer's Association: July 2014 Volume 10, Issue 4, Supplement, Page P399

67. Amyloid PET Screening for Enrollment into Alzheimer's Disease Clinical Trials: Initial Experience in a Phase 1b Clinical Trial
Jeff Sevigny, Joyce Suhy, Ping Chiao, Klein, Joonmi Oh, Derk Purcell, Mehul Sampat, Jerome Barakos
Neurology April 8, 2014 vol. 82 no. 10 Supplement P3.207
American Academy of Neurology, 66th AAN Annual Meeting April 26- May 03, 2014: Philadelphia, PA 2014

IN THE HEALTH CARE ALTERNATIVE DISPUTE RESOLUTION OFFICE

TAMMIE FRALEY, Individually, and as Personal Representative of the ESTATE OF JESSICA HAYNES, *et al.*, Claimants, *v.* MERITUS MEDICAL CENTER, INC., *et al.*, Health Care Providers.	Case No.

CERTIFICATE OF QUALIFIED EXPERT

I, David H. Goldstein, M.D., do hereby certify and affirm that:

1. I am Board Certified in internal medicine and pulmonary medicine and have had clinical experience in the field of internal medicine, pulmonology, and as a hospitalist within the past five years of the date of the events which form the basis of this litigation. My Attesting Report and *curriculum vitae* are attached hereto.

2. I have reviewed medical records pertaining to Jessica Haynes regarding health care services rendered by Berkeley Medical Center, Meritus Medical Center, War Memorial Hospital, Ruby Memorial Hospital, and Select Specialty Nursing Home. I have also reviewed the Certificate of Qualified Expert and Attesting Report of Jerome Barakos, M.D.

3. Based upon my education, training, and experience in internal medicine and as a hospitalist as well as the medical records and information provided in this case, it is my opinion, within a reasonable degree of medical probability that the hospitalists involved in the care of Ms. Haynes at Meritus Medical Center who are identified in my attached report violated the standard of care.

4. I do not spend more than 20% of my professional time on medical legal matters.

DATE: 5/27/18

David H. Goldstein, M.D.

IN THE HEALTH CARE ALTERNATIVE DISPUTE RESOLUTION OFFICE

TAMMIE FRALEY, Individually, and as Personal Representative of the ESTATE OF JESSICA HAYNES, *et al.*, Claimants, *v.* MERITUS MEDICAL CENTER, INC., *et al.*, Health Care Providers.	Case No.

ATTESTING EXPERT REPORT

My name is David H. Goldstein, M.D. and I am a board certified physician in Internal Medicine and Pulmonary Medicine. I also perform medical services as a Hospitalist. It is my opinion to within a reasonable degree of medical certainty that the Healthcare Providers rendering care to Jessica Haynes at Meritus Medical Center on the Hospitalist team violated the standard of care by failing to include on their differential diagnosis a brain abscess and to appropriately rule in or out the various conditions on their differential diagnosis. It is also my opinion that those same healthcare providers violated the standard of care in failing to obtain an MRI study subsequent to July 6 and prior to discharge. It is further my opinion that the same healthcare providers violated the standard of care in failing to consult with a neurosurgeon for treatment. According to the medical records, the healthcare providers whose care falls under the category of the "hospitalist team," whom I am critical, include the following: Brad Young, PA-C; Dr. Njomo; Dawit Wubie, M.D.; Chintu Sharma, M.D; Sherry Baldassari, N.P.; Elizabeth Konadu, M.D.; and others whose names may not yet be discernable from the records.

Within a reasonable degree of medical certainty, as a female in her thirties who presented with an abnormal headache, leukeoctosis, an abnormal lumbar puncture, and a localized brain lesion, the standard of care required a brain abscess to be placed on the differential diagnosis and to be worked up and ruled in/out. While it was reasonable to initially place a stroke on the differential diagnosis, had this been a stroke, within a reasonable degree of medical certainty, this lesion would have gotten smaller over time. Given the fact that the lesion grew throughout the admission as documented in the medical records as well as the opinion rendered by Dr. Barakos that a subsequent MRI between June 6 and her discharge would have more likely than not shown continued growth of the lesion, the standard of care required that a stroke be eliminated from the differential diagnosis and that the hospitalists and internists placed a stronger emphasis on a diagnosis of an abscess

that required, at a minimum, repeat MRI studies to confirm the presence of an abscess and a consultation with neurosurgery to explore the available surgical treatment options with the patient.

This is a preliminary report and if new information is brought to my attention, I may revise, expand, or otherwise amend my opinions prior to any trial.

DATE: 5/24/18

David Goldstein, M.D.

CURRICULUM VITAE

David H. Goldstein, M.D.

BACKGROUND:

Born:	Winnipeg, Manitoba, Canada
Citizenship:	United States Citizen
Marital Status:	Married
Children:	Two

EDUCATION:

1976	Bachelor of Science-Research Medicine University of Manitoba, Winnipeg, Manitoba, Canada
1976	Doctor of Medicine University of Manitoba, Winnipeg, Manitoba, Canada

HOSPITAL AND ACADEMIC POSITIONS:

1976-77 Medical Intern-Peter Bent Brigham Hospital
Harvard Medical School-Boston, Massachusetts

1977-78 Junior Resident-Medicine-Peter Bent Brigham Hospital
Harvard Medical School-Boston, Massachusetts

1978-79 Senior Resident-Medicine-Peter Bent Brigham Hospital-
Harvard Medical School-Boston, Massachusetts

1977-78 Pulmonary Fellow-Harvard School of Public Health-
Harvard Medical School-Boston, Massachusetts

1979-80 Pulmonary Fellow-Peter Bent Brigham Hospital-
Harvard Medical School-Boston, Massachusetts

Currently: Assistant Clinical Professor of Internal Medicine, Florida State University Medical School

Currently: Assistant Clinical Professor of Pulmonary Medicine, Florida State University Medical School

Currently: Assistant Clinical Professor of Hospitalist Medicine, Florida State University Medical School

OTHER ACTIVITIES:

Currently	Pulmonologist and Hospitalist at Sarasota Memorial Hospital, Sarasota

Periodically	Private Practice Wound and Hyperbaric Medicine at Memorial Hospital Wound Center, Tampa, Florida
1980-2005	Private Practice-Pulmonary Medicine and Internal Medicine, Tampa, Florida
1993-2002	Chief Financial Officer Tampa Medical Research Associates, Inc.,Tampa, Florida
1984- Present	Review coal miner's pneumoconiosis cases for Department of Labor. Reviewed over 100 cases.

EXAMINATIONS:

Examinations	Place Written	Date Passed
LMCC Winnipeg		1976
National Board Exams	Boston	1979
American Board of Internal Medicine	Miami	1980
American Board of Pulmonary Medicine	Tampa	1982

AWARDS:

Name	Date Received
Governor General's Award of Canada	June 1970
Actuarial Award of Manitoba	June 1970
Manitoba Centennial Scholarship	June 1970
Buller Biology Award	June 1971
First Standing Scholarship (Science)	June 1972
Research Thesis Award (Medicine)	June 1974
Research Presentation Award (Medicine)	June 1974
Gold Medal Medical Achievement	June 1976

PRESENTATIONS:

Title	Place	Date
"Importance of Phase Angle in the Measure of Forced Oscillatory Impedance"	UTMB (Galveston)	April 1975
"Total Respiratory Impedance Immediately after Panting"	FASEB (Dallas)	April 1979

"Use of Magnetometers to Volume Reference Flow-Volume Curves" ATS (Las Vegas) May 1979

LICENSURE: Florida-Medical Doctor #ME 0035805

PUBLICATIONS:

A.J. Ross, M.D. Raber, B.W. Kirk, D.H. Goldstein: Direct Readout of Respiratory Impedance. Medical and Biological Engineering, September 1976, pp. 558-564.

D.H. Goldstein, J. Mead: Total Respiratory Impedance After Panting. Abstract, Federation Proceedings, April 1979, #6417, pp. 1445.

D.H. Goldstein, J. Mead: The use of Magnetometers to Volume-Reference Flow Volume Curves. Abstract, American Thoracic Society Proceedings, May, 1979, pp. 312.

D.H. Goldstein, J. Mead: Total Respiratory Impedance After Panting. The Journal of Applied Physiology, 1980, pp. 1024-1028.

D.H. Goldstein, J. Mead: Use of Magnetometers of Flow-Reference Flow Volume Curves. The Journal of Applied Physiology, 1980, pp. 731-736.

T. H. Rossing, C.H. Fanta, D. H. Goldstein, J.R. Snapper, E.R. McFadden, Jr.: Emergency Therapy of Asthma: Comparison of the Acute Effects of Parenteral and Inhaled Sympathomimetic and Infused Aminophylline. American Review of Respiratory Disease, Volume 122, 1980, pp. 365-371

D.H. Goldstein, As.S. Slutsky, R. H. Ingram, Jr., P. Westerman, J. Venegas and J Drazen: CO2 Elimination by High Frequency Ventilation (4-10Hz. In Normal Human Subjects. American Review of Respiratory Disease. March 1981, Volume 12, Number 3, pp. 251-255.

INVESTIGATIONAL ACTIVITIES:

1987-1988	Nifedipine GITS investigational hypertension drug study. **Pfizer Pharmaceuticals**
1988-1990	Azelastine investigational asthma drug study. **Wallace Pharmaceuticals**
1989-1990	Nifedipine single dose investigational hypertensive drug study. **Miles Pharmaceuticals**
1989-1990	Cefaclor A.F. vs Cefaclor in various bacterial infections. **Eli Lilly Pharmaceuticals**
1990-1992	Double blind, randomized trial comparing effects of Captopril and Enalapril on Quality of Life in older hypertensive patients. **Squibb Pharmaceuticals**
1990-1991	Cefpodoxime Proxetil vs Cefaclor in treatment of "community acquired" pneumonia. **Upjohn Pharmaceuticals**
1990-1991	Multiple comparisons of the combination of Ipratropium Bromide and Albuterol with its components in a 12-week parallel study in adults with COPD. **Boehringer-Ingelheim Pharmaceuticals**

1990-1991	Safety of once daily Nisoldipine Coat-core 20mg., 40mg., and 60 mg. tablets vs placebo in patients with stable exertional angina pectoris. **Miles Pharmaceuticals**
1991-1991	Comparative safety and efficacy of Clarithromycin and Cefaclor in treatment of acute exacerbation of bronchitis. **Abbott Labs**
1991-1991	Treatment of Rheumatoid or Osteo-Arthritis, NSAIDS vs Nabumetone. **SmithKline Beecham**
1991-1992	Double blind study of efficacy of injectable Calcitonin in treatment of glucocorticoid-induced osteoporosis. **Rhone-Poulenc Rorer**
1991-1992	A double-blind, multiple-dose, crossover, dose comparison trial of Formoterol Suspension Aerosol vs Placebo in patients with reversible obstructive airways disease. **Ciba-Geigy**
1991-1992	Dose Ranging: Six Weeks' Therapy with oral ICI204,219 in bronchial asthma. **ICI Pharmaceuticals**
1991-1993	Study of efficacy, safety and tolerability of short course therapy with Azithromycin in treatment of upper and lower respiratory tract infections. **Pfizer Labs**
1992-1993	Double-blind, randomized multi-center study of C1983 in the treatment of community-acquired bacterial pneumonia. **Parke-Davis**
1992-1993	Loracarbef vs Ceftin in acute exacerbation of chronic bronchitis. **Lilly**
1992-1993	Multi-center, double-blind, placebo controlled Phase II study to evaluate Safety and efficacy of aerosolized rhDNase in hospitalized patients with chronic bronchitis experiencing an acute exacerbation. **Genentech**
1992-1994	Double-blind, Phase III evaluation of Doxophylline, Theophylline and placebo in patients with reversible asthma. **Roberts Pharmaceuticals**
1992-1994	Phase III study of effects of Zileuton 400 mg. q.i.d. and 600 mg. q.i.d. vs Theophylline in treatment of moderate asthma. **Abbott**
1993-1993	Phase II study of safety and efficacy of aerosolized rhDNase in patients with bronchiectasis. **Genentech**
1993-1994	Comparison of efficacy, safety and tolerance of Ceftibuten 300 mg. b.i.d. and Augmentin 500 mg. t.i.d. in treatment of community-acquired pneumonia. **Schering-Plough**
1993-1994	Comparison and efficacy, safety and tolerance of Ceftibuten 400mg.

	in fed and fasted state and Augmentin Amoxicillin/Clavulanate in treatment of acute exacerbation of chronic bronchitis. **Schering Plough**
1993-1994	A prospective, randomized, double-blind comparative study of Ciprofloxacin and Cefuroxime Axetil in treatment of acute bacterial exacerbation of chronic bronchitis. **Miles**
8/93-10/93	A dose Response Study of in asthma. **Rhone-Poulenc Rorer**
9/93-12/94	Insomnia treatment study comparing Triazolam and Temazepam. **Upjohn**
10/93-1/94	Double-blind, placebo controlled, parallel group study to evaluate two (2) dose levels (10 & 20mg.) of intranasal Sumatriptan in acute treatment of a migraine attack. **Glaxo**
11/93-11/94	Multi-center, randomized, double-blind, placebo controlled, parallel group study of the safety of inhaled corticosteroid sparing effect of Azelastine in inhaled corticosteroid-dependent asthmatics. **Wallace Pharmaceuticals**
11/93-4/95	Double-blinded, randomized, multi-center clinical trial comparison of safety and efficacy of Ciprofloxacin vs. Clarithromycin in treatment of patients with an acute exacerbation of chronic bronchitis. **Miles Pharmaceuticals**
11/93-2/95	Double-blinded, randomized, multi-center clinical trial comparison of safety and efficacy of Ciprofloxacin vs. Clarithromycin in treatment of patients with acute sinusitis. **Miles Pharmaceuticals**
11/93-1996	Randomized, placebo controlled trial of E5 Antiendotoxin Monoclonal antibody in patients with severe sepsis. **Pfizer**
11/93-1996	Three-arm comparison trial for treatment of MAC Bacteremia in AIDS: a Clarithromycin/Ethambutol regimen containing Rifabutin 900 mg. or 600 mg. or placebo. **Adria**
2/94-9/94	Randomized, double-blinded, double-dummy, placebo-controlled, comparative clinical trial of Salmeterol via multi-dose powder inhaler vs Salmeterol via Diskhaler for four weeks in adolescent and adult subjects with mild to moderate asthma.(SLGA2004) **Glaxo**
03/94-10/94	Randomized, double-blind trial comparing 10 days oral therapy with CP-99,219 or cefaclor for the treatment of uncomplicated, community acquired pneumonia. **Pfizer**
03/94-07/94	Randomized, double-blind trial comparing 10 days oral therapy with CP-99, 19 or ofloxacin for the treatment of acute exacerbation of chronic bronchitis. **Pfizer**
6/94-1/95	Dose ranging study of oral Bidisomide vs. placebo in reducing the recurrence of symptomatic supraventricular tachycardia. **Searle**
7/94-1/95	Randomized, double-blind, placebo controlled study to evaluate

	headache pain relief with Sumatriptan Nasal Spray 5mg., 10mg., and 20mg. across three migraine attacks. **Glaxo, Inc.**
11/94-9/95	Multinational, multi-center, double-blind, placebo controlled Phase III study to evaluate efficacy and safety of aerosolized recombinant human DNase I in hospitalized patients with chronic obstructive pulmonary disease experiencing a pulmonary exacerbation. **Genentech**
1/95-1/96	Multiple dose comparison of Ipratropium Bromide HFA-134a and Ipratropium Bromide CFC in a 12-week, double-blind, parallel group study in adults with chronic obstructive pulmonary disease. **Boehringer-Ingelheim.**
11/94-4/95	A two-way crossover clinical study of two Beclomethasone Dipropionate metered-dose inhalers in the treatment of stable, steroid-dependent asthma. **Novopharm**
7/95-1/96	A twelve-week, double-blind, parallel group trial comparing the safety, tolerability and efficacy of Formoterol Dry Powder Capsules for inhalation delivered by a single-dose I Inhaler vs Albuterol Metered-Dose Inhaler (MDI) vs placebo in patients with mild to moderate asthma. **Ciba-Geigy**
8/95-7/96	A randomized, double-blind, double-dummy, comparative clinical trial of Salmeterol 50mcg. b.i.d. via the Diskus and Salmeterol 50 mcg. b.i.d. via the metered-dose inhaler vs placebo for twelve weeks in adolescent and adult subjects with mild to moderate asthma. (SLGA3011) **Glaxo-Wellcome**
8/95- Feb 1998	A randomized, double blind, placebo-controlled, 4X5 factorial trial of Telmisartan and Hydrochlorothiazide in patients with mild to moderate essential hypertension. **Boehringer-Ingelheim**
6/95-12/96	A randomized, double-blind, placebo controlled crossover study to evaluate the efficacy of oral Naratriptan in the acute treatment of four migraine attacks. **Glaxo-Wellcome**
8/95-10/96	A trial of Recombinant Methionyl Human Brain-Derived Neurotrophic Factor (r-metHuBDNF) given by daily subcutaneous injection to patients with Amyotrophic Lateral Sclerosis (ALS) **Amgen**
8/96-7/97	A randomized, double-blind, parallel-group, 12-week study to evaluate the safety and efficacy of switching from Albuterol 200 mcg. (180mcg. Ex-Actuator) in CFC propellant 11 and 12 administered q.i.d. to Albuterol 200 mcg. (180 mcg. Ex-Actuator) in GR 106642X propellant administered q.i.d. and to Albuterol 200 mcg. (180 mcg. Ex-Actuator) in GR 106642X propellant administered as needed in adult subjects with asthma. (SALA3002) Glaxo Wellcome Inc.
11/96- Feb 1998	Prospective, Randomized, Double-Blind Comparison of the Safety

	and Efficacy of Bay 12-8039 400mg QD X 10 Days vs. 400mg QD X 5 days vs. Clarithromycin 500mg BID X 10 days for the Treatment of Patients with Acute Exacerbations of Chronic Bronchitis. (D96-027) **Bayer Pharmaceuticals.**
9/96- 10/97	The effects of Theophylline on breathlessness and general health status in patients with chronic obstructive pulmonary disease: A multi-investigator study. **Purdue Frederick Company**
1/95-1996	A placebo-controlled, double-blind, dose-ranging study of Azmacort HFA-134a Oral Inhaler compared to Azmacort Oral Inhaler in the treatment of asthma (Pr. RG 5016T-201) **Rhone-Poulenc Rorer Pharmaceuticals, Inc.**
11/95-7/97	A multicenter, randomized, double-blind placebo controlled trial of Zafirlukast (Accolate) in subjects with mild to moderate asthma: 3 weeks extension (Pr. 9188IL/0060 : 0011) **Zeneca Pharmaceuticals**
1/95-6/97	A multicenter, randomized, double-blind, parallel-group, 12-week trial comparing two doses of Zafirlukast (Accolate) in combination with low-dose inhaled Corticosteroids versus high-dose inhaled corticosteroids alone in subjects with mild-to moderate asthma. (9188IL/0094) **Zeneca Limited**
1/96-1/97	A six-week, double-blind, parallel-group, dose-ranging trial comparing the safety, tolerability, and efficacy of four different dose levels of Iralukast (CGP 45 715 A) dry powder capsules for inhalation versus placebo in patients with mild to moderate asthma. (Pr. 45715 01 004) **Ciba Pharmaceuticals**
1/96-3/96	A randomized, double-blind, double-dummy, comparative clinical trial of twelve week courses of Salmeterol Xinafoate versus Ipratropium Bromide versus Placebo (prn Ventolin) in subjects with chronic obstructive pulmonary disease. **(SLGA4004) Glaxo**
1996-8/97	A phase II, multi-center, double-blind, placebo-controlled study to evaluate the safety and efficacy of anti-IgE recombinant humanized monoclonal antibody (rhuMaB-E25) in patients with moderate-severe allergic asthma. (Q0694g) **Genentech, Inc.**
3/97-11/98	A 12-month, double-blind, between-patient, placebo-controlled trial comparing the safety, tolerability and efficacy of 12ug and 24ug twice-daily Formoterol dry powder capsules for inhalation delivered by a single-dose inhaler (Aeroliser^{tm}) in children with asthma in need of daily treatment with inhaled bronchodilators and anti-inflammatory treatment. (Pr. 049) Novartis
6/97-Feb 1998	A Comparison of Salmeterol Versus Theophylline Versus Salmeterol plus Theophylline in COPD patients. (SLGA4020) **Glaxo-Wellcome**
July 1997 - 03/99	A Randomized, Double-Blind, Placebo-Controlled Comparative

	Trial of Fluticasone Propionate 440mcg BID or 880mcg BID versus Placebo Administered Via Metered Dose Inhaler in Propellant 11/12 or GR106642X in Adolescent and Adult Oral Corticosteroid-Dependent Asthmatics (FLTA3022) **Glaxo-Wellcome**
Nov 1997 - Feb 98	A 12-week Comparison of Daily Doses of 100mcg and 200mcg of HFA-134A Beclomethasone Dipropionate (BDP) versus Placebo in Pediatric Patients with Symptomatic Asthma (1167-BRON) **3M Pharmaceuticals**
Oct 1997 - Dec 97	A Randomized, Double-Blind, Parallel Group, Comparison of Inhaled Salmeterol Xinafoate (42mcg BID) With Oral Zafirlukast (20mg BID) in Subjects with Mild to Moderate Asthma (SLGA5025) **Glaxo-Wellcome**
Nov 1997 - Mar 99	A Randomized, Between-Patient Trial Comparing Two doses of Inhaled Formoterol Fumarate Dry Powder (12ug and 24ug) with Placebo (Double-Blind) and with Oral Slow-Release Theophylline at Individual Doses Based on Serum Levels (Open-Label), each Administered Twice Daily for one year to Patients with Chronic Obstructive Pulmonary Disease in terms of Clinical Efficacy, Tolerability and Quality of Life. (Protocol 058) **Novartis**
Dec 1997 - 10/98	A Randomized, Double-Blind, Double-Dummy, Parallel Group, Comparative Study of Inhaled Fluticasone Propionate 88mcg BID Versus Zafirlukast 20mg BID in Asthmatic Subjects who are Currently Receiving Low Dose Inhaled Corticosteroids (FLTA4035) **Glaxo-Wellcome**
Nov 1997 - Apr 98	A Double-Blind, Randomized, Placebo Controlled Study of GS4104 in the Treatment of Influenza Infection (GS-97-803) **Gilead Sciences**
Nov 1997 - Jul 98	Placebo-Controlled Efficacy and Safety Study with Long-Term Safety Evaluation of Mometasone Furoate HFA-227 Metered Dose Inhaler in the Treatment of Asthma in Subjects Previously Maintained on Inhaled Beta-Agonists (C97-223-06) **Schering-Plough Research Institute**
Feb 1998 - 12/98	A Comparative Study of the Efficacy of Clarithromycin and Azithromycin for the Treatment of Patients with Acute Exacerbation of Chronic Bronchitis (M97-766) **Abbott Labs**
Feb 1998 - 12/98	A Comparative Study of the Efficacy and Safety of Clarithromycin and Loracarbef for the Treatment of Patients with Secondary Bacterial Infections of Acute Bronchitis (M97-752) **Abbott Labs**
Feb 1998 - Jul 98	Prospective, Randomized, Double-Blind, Comparison of the

	Safety and Efficacy of Oral Moxifloxacin (Bay 12-8039) 400mg QD for Ten Days Versus Oral Cefuroxime Axetil 250mg BID for Ten Days For the Treatment of Patients with Acute Bacterial Maxillary Sinusitis (Protocol 100107) **Bayer Corp.**
May 1998 - 1/99	Dose Response Comparison of HFA-134a Beclomethasone Autohaler [tm] Inhalation Device with HFA-134a Beclomethasone Press & Breathe MDI In Patients with Asthma (1273-BRON) **3M Pharmaceuticals**
June 1998 - 11/98	Study to Evaluate the Effect of EM574 5mg QID, 10mg TID, 20mg BID versus Placebo in Females with Non-Erosive Gastroesophageal Reflux Disease (EM97032) **TAP Holdings.**
July 1998 - 6/99	A Multicenter, Randomized, Double-Blind, Comparative study of oral HMR3647 (800mg Once Daily) versus oral Cefuroxime Axetil (500mg Twice Daily) for Outpatient Treatment of Acute Exacerbation of Chronic Bronchitis in Adults.(HMR3647A/3007) **Hoechst Marion Roussell.**
October 98 - 6/99	Randomized, parallel-group, open-label, multicenter, clinical study comparing the safety, efficacy, quality of life and socioeconomic variables of twice daily formoterol powder (12ug bid) to twice daily salmeterol (50ug bid) administered for six months to adult subjects with reversible obstructive airway disease (ROAD)., Protocol 073, NOVARTIS
September 98- 4/00	A Randomized, double-blind, placebo-controlled, parallel-group Trial Evaluating the Safety and Efficacy of the DISKUS Formulations of Salmeterol 50mcg BID and Fluticasone Propionate 500mcg BID Individually and in Combination as Compared to Placebo in COPD subjects. Protocol SFCA3006, **Glaxo-Wellcome**
November 98-4/99	A Multi-Center, Double-blind, Placebo-Controlled, Parallel-Group, Dose-Ranging (0.25 to 10mg) Clinical Evaluation of Oral GI262570X as a Monotherapy for 12 Weeks Duration in Subjects with Type 2 Diabetes Mellitus Protocol PPA20005 **Glaxo-Wellcome**
January 99 - 9/99	A Randomized, Double-Blind, Double Dummy, Parallel Group Comparison of Salmeterol Xinafoate Inhalation Powder (50mcg BID) with Oral Montelukast (10mg QD) in Subjects with Persistent Asthma Symptomatic on Concomitant Inhaled Corticosteroid Therapy. Protocol SMS40004 **Glaxo-Wellcome**
March 99 - 11/99	A Randomized,Double-Blind, Parallel Group Comparison Study of Inhaled Fluticasone Propionate (88mcg BID) Versus Montelukast Sodium (10mgQD) in Subjects Currently Receiving Beta Agonists Alone. Protocol. FLTA4038 **Glaxo-Wellcome**
April 99 - 10/99	Safety and Efficacy Study of HFA-134a Albuterol Sulfate

Delivered from a Press-and-Breathe MDI, HFA-134a

Albuterol Sulfate Delivered from the Autohaler^{tm} Inhalation Device, and HFA-placebo in Patients with Asthma. Protocol 1332-SILV. **3M Pharmaceuticals**

August 99 - 1/00 — A Randomized, Double-Blind, Multicenter Study to evaluate the Tolerability and Effectiveness of Rofecoxib (MK-0966) 25mg q.d. vs. Naproxen 500mg b.i.d. in Patients with Osteoarthritis. Protocol 102-00 **MERCK**

August 99 - 2/00 — Phase II Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy, Safety, and Tolerability of Six Weeks Treatment by Oral Dosing with CJ-13,610 in Adults with Chronic Obstructive Pulmonary Disease. Protocol A2531002, **PFIZER**

September 99 - 5/2001 — A Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Clinical Evaluation of GI262570 Sodium Tablets (2.5mg, 5mg, 7.5mg) as a Monotherapy for 26 Weeks in Subjects with Type 2 Diabetes Mellitus Protocol 30013 **GLAXO-WELLCOME**

October 99 - 4/2001 — A Multicenter, Randomized, Double-Blind, Double-Dummy, Parallel-Group, Glyburide-Controlled 12-Month Clinical Evaluation of Oral GI262570 7.5mg Alone, Micronized Glyburide 12mg Alone, or Micronized Glyburide 12mg in combination with GI262570 (2.5mg, 5mg or 7.5mg) Administered to Subjects with Type 2 Diabetes Mellitus who are Inadequately Controlled on Maximum Dose Glyburide. Protocol 30001 **GLAXO-WELLCOME**

October 99 - 3/00 — A Double-Blind, Randomized, Placebo-Controlled, Parallel-Group, Multi-Center Study to Investigate the Efficacy and Safety of Inhaled Zanamivir 10mg Administered Twice Daily for Five Days in the Treatment of Influenza in Patients 12 years or over Diagnosed with Asthma or Chronic Obstructive Pulmonary Disease (COPD). Protocol NAI30008 **GLAXO-WELLCOME**

February 00 - 8/2001 — A Randomized, Double-Blind Multicenter Study to Evaluate the Effect of Adding Either Montelukast Sodium or Salmeterol Xinafoate to Inhaled Fluticasone in Adult Asthmatics. Protocol 120-01 **MERCK**

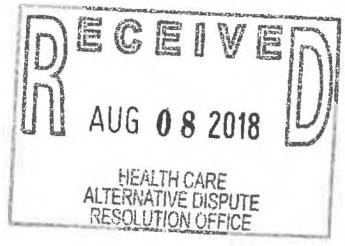
March 00 - 8/2000 — A Randomized, Double-Blind, Double-Dummy, Parallel Group, 12-Week Comparative Trial of Salmeterol/ Fluticasone Propionate Combination Product 50/100mcg BID via the DISKUS Inhaler Versus Oral Montelukast 10mg QD in Adolescents and Adults with Persistent Asthma. Protocol SAS40020 **GLAXO-WELLCOME**

April 00 - 1/2002 — A Randomized, Double-Blind, Parallel Group, Comparative

	Trial of Salmeterol/Fluticasone Propionate Combination Product 50/100mcg DISKUS Inhaler BID versus Fluticasone Propionate 250mcg DISKUS Inhaler BID In Adolescents & Adults with Moderate Persistent Asthma. Protocol SAS40026 **GLAXO-WELLCOME**
01/2001 - Ongoing	An Obversational Study of the Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR-Q2196n) **Genentech, Inc.**
08/2000 - Ongoing	A Multicenter, Randomized, Controlled, Open-Label Study to Evaluate the Safety of Xolair in Moderate to Severe Persistent Asthma Subjects already treated with other Therapies (ALTO-Q2143g) **Genentech, Inc.**
10/2000 - 8/2001	A One-Year Randomized, Double-Blind, Placebo and Active-Controlled Parallel Design Safety and Efficacy Comparison of Combivent HFA Inhalation Aerosol to Combivent (CFC) Inhalation Aerosol in Patients with COPD. (1012.11) **Boehringer-Ingelheim.**
01/2001 - Ongoing	A Multi-Center, Randomized, Double-Blind, Double-Dummy,Parallel Group, 8 Week Comparison of Salmeterol XinafoateVersus Ipratropium Bromide Versus Salmeterol Xinafoate plus Ipratropium Bromide Versus Placebo in Subjects withChronic Obstructive Pulmonary Disease. (SMS40315) **Glaxo Wellcome.**
02/2002 - Ongoing	A Multi-center, Randomized,Double-Blind, Double-Dummy, Parallel-Group, 16-week Comparison of Asthma Control in Adolescents andAdults Receiving Either Fluticasone Propionate/Salmeterol Diskus Combination Product 100/50 mcg BID, Fluticasone Propionate Diskus 100mcg BID, Salmeterol Xinafoate Diskus 50mcg BID, or or Oral Montelukast 10mg QD. SAS40036 **GlaxoSmithKline**
12/2001 - Ongoing	A Randomized, Double-Blind, Double-Dummy, Parallel Group, Comparative Clinical Trial Evaluating Fluticasone Propionate/Salmeterol Xinafoate (250/50mcg BID via Diskus) to Ipratropium Bromide/Albuterol Sulfate (36mcg/ 206mcg QID) Inhalation Aerosol in Subjects with Chronic Obstructive Pulmonary Disease SCO40012 **GlaxoSmithKline**
5/21/2001 - 4/2002	A Phase II, Randomized, Placebo-Controlled, Double-Blind, Parallel-Group, Dose-Finding Study to Evaluate the Effectiveness of 28 days of Treatment with LDP-977 in Adult Asthmatics.(M97700-023) **Millennium Pharmaceuticals, Inc.**

IN THE HEALTH CARE ALTERNATIVE DISPUTE RESOLUTION OFFICE

TAMMIE FRALEY, Individually, and as Personal Representative of the ESTATE OF JESSICA HAYNES, *et al.*, Claimants, *v.* MERITUS MEDICAL CENTER, INC., *et al.*, Health Care Providers.	Case No.



CERTIFICATE OF QUALIFIED EXPERT

I, Matthew Ammerman, M.D., do hereby certify and affirm that:

1. I am Board Certified in neurosurgery and have had clinical experience in the field of neurosurgery within the past five years of the date of the events which form the basis of this litigation. My Attesting Report and *curriculum vitae* are attached hereto.

2. I have reviewed medical records pertaining to Jessica Haynes regarding health care services rendered by Berkeley Medical Center, Meritus Medical Center, War Memorial Hospital, Ruby Memorial Hospital, Select Specialty Hospital, Shenendoah Center, Brightwood Center, as well as the radiology studies from Meritus Medical Center, the Death Certificate, and Dr. Barakos' report.

3. Based upon my experience in neurosurgery as well as the medical records and information provided in this case, it is my opinion, within a reasonable degree of medical certainty that had the standard of care been adhered to and a neurosurgeon been consulted while Ms. Haynes was admitted to Meritus Medical Center, if neurosurgery wasn't available a transfer should have been immediately made. She would have then undergone surgical treatment that would have resulted in a successful outcome and would not have incurred the subsequent medical care she endured and her ultimate death.

4. I do not spend more than 20% of my professional time on medical legal matters, nor is my compensation from such matters more than 20% of income.

DATE: 6-19-18

IN THE HEALTH CARE ALTERNATIVE DISPUTE RESOLUTION OFFICE

TAMMIE FRALEY, Individually, and as Personal Representative of the ESTATE OF JESSICA HAYNES, *et al.*, Claimants, *v.* MERITUS MEDICAL CENTER, INC., *et al.*, Health Care Providers.	Case No.

ATTESTING EXPERT REPORT

My name is Matthew Ammerman, M.D. and I am a board certified Neurosurgeon and currently practice Neurosurgery in the District of Columbia. My *curriculum vitae* is attached hereto.

It is my opinion to within a reasonable degree of medical certainty that had a neurosurgeon been consulted regarding the care of Jessica Haynes while she was admitted to Meritus Medical Center and if not available a transfer made emergently, she would have undergone surgical intervention and would have had a successful outcome and would not have passed away.

Specifically, it is my opinion within a reasonable degree of medical probability that an abscess should have been on the working differential diagnosis once the results of the spinal tap were available. Additionally, a neurosurgery consultation should have been requested no later than June 6, 2016 after the MRI was reported and identified an enhanced ring. In this patient, had a neurosurgeon been consulted, the standard of care would have required and did in fact require that she be placed on a regimen of triple antibiotics and stereotactic aspiration should have been conducted while this patient was admitted to Meritus Medical Center. Within a reasonable degree of medical certainty, had Ms. Haynes undergone such surgical intervention at any point in time that she was admitted at Meritus Medical Center, she not only would have survived, but she would have only suffered neurological deficits similar to those that she initially presented with such as right upper extremity hemiparesis that would have improved over time and speech deficits that would have improved over time. Additionally, if there was not a neurosurgeon available at Meritus Medical Center to conduct the surgical intervention required, the standard of care required that she should have been transferred to a higher

level of care facility that was capable of conducting such a procedure and following the standard of care as identified above, which, within a reasonable degree of medical certainty, would have resulted in not only her survival, but would have only left her suffering neurological deficits similar to those that she initially presented with such as right upper extremity hemiparesis that would have improved over time and minor speech deficits that would have improved over time

This is a preliminary report and if new information is brought to my attention, I may revise, expand, or otherwise amend my opinions prior to any trial.

DATE: 6-19-18

Matthew Ammerman, M.D.

CURRICULUM VITAE

MATTHEW DAVID AMMERMAN

6526 Elgin Lane
Bethesda, MD 20817
301-469-7275(H).
wnalegal@gmail.com

Birth and Citizenship:

DOB: Washington, DC
US Citizen

Private Practice in Neurological Surgery at:

Washington Neurosurgical Associates, PC
5215 Loughboro Road, NW
Suite #510
Washington, D.C. 20016
(202)966-6300 (0)
(202)364-4362 (f)
www.neurosurgerydc.com

Clinical Appointments:

Assistant Clinical Professor of Neurological Surgery at George Washington University
Adjunct Assistant Clinical Professor of Neurological Surgery at Johns Hopkins

Education:

College:	Emory University, Atlanta, GA August 1994-May 1998; B.S. with Summa Cum Laude in biology
Medical School:	George Washington University Washington, DC, August 1998-May 2002 MD with Distinction

Mortar Board, 1998
Order of Omega, Greek Honor Society (Member and President), 1996-98
Emory College Deans' List – 8 semesters
Washingtonian Top Doctor - 2012, 2014, 2016

Courses:

Course Instructor for – Microsurgical Techniques: A Hands on course 11/13/99 – 11/14/99. George Washington Neurological Institute and Ammerman Neurosurgical Laboratory, Washington, DC.

Invited Faculty - Spine + Science + Management: teaching residents and fellows DLIF techniques 4-22-2010 to 4-24-2010. Miami Florida, JW Marriott.

Invited Faculty - MAST Techniques Custom Training April 8, 2011. MERI, Memphis, TN.

Invited Faculty - MAST Techniques and training Sept 15-16th, 2011. MERI, Memphis, TN.

Invited Faculty - Spine + Science + Management: teaching residents and fellows MAST techniques 4-28-2011 to 4-30-2011. Miami Florida, JW Marriott

Invited Faculty - Spine + Science + Management: teaching resident and fellows MAST techniques 5-2-2013 to 5-3-2013. Tampa Florida

Invited Faculty - Spine + Science + Management: teaching residents and fellows MAST techniques 5-16-2014 to 5-17-2014

Invited Faculty - Spine + Science + Management: teaching residents and fellows MAST techniques 5-15-2015 to 5-17-2015

Invited Faculty -Spine + Science + Management: teaching residents and fellows MAST techniques 5-20-2016 to 5-22-2016

Invited Faculty -Spine + Science + Management: teaching residents and fellows MAST techniques 5-12-2017 to 5-13-2017

Texts and Book Chapters:

Internship:	George Washington University Medical Center Department of Surgery Washington, D.C. July 2002-June 2003 Director: Paul Lin, M.D.
Residency:	George Washington University Medical Center Department of Neurosurgery Washington, D.C. July 2003 to June 2008 Director: Anthony J. Caputy, MD
Fellowship:	University of Tennessee Semmes-Murphey Clinic Minimally Invasive and Complex Spine Surgery Memphis,TN July 2008 to June 2009 Director: Kevin T. Foley, MD

USMLE:

Step 1 (passed 6/13/00)
Step 2 (passed 2/01/02)
Step 3 (passed 9/22/03)

ABNS:
Written exam (passed 3/25/2006)
Board Certified (11/27/2013)

Medical License:

Washington DC	MD036651 exp 12/2018
Tennessee	MD43435 (retired)
Florida	ME117676 exp 01-31-2018

Awards and Honors:

Wolfgang Koos, MD Neurosurgical Resident's Award, 2005
William Beaumont Society
Gill Fellowship Award 2001
Omicron Delta Kappa Leadership Honor Society (Member and President), 1997-98

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Ernest Senz, **Matthew Ammerman**, Mark Grant, Damirez Fossett. "Chapter 31-Carpal Tunnel Release." Operative Neurosurgical Anatomy. Damirez Fossett MD and Anthony Caputy MD, Ed. Thieme Publications: New York, NY. January 2002.

Ernest Senz, **Matthew Ammerman**, Damirez Fossett. "Chapter 32-Radial Nerve Decompression." Operative Neurosurgical Anatomy. Damirez Fossett MD and Anthony Caputy MD, Ed. Thieme Publications: New York, NY. January 2002.

Ernest Senz, **Matthew Ammerman**, Damirez Fossett. "Chapter 33-Ulnar Nerve Decompression." Operative Neurosurgical Anatomy. Damirez Fossett MD and Anthony Caputy MD, Ed. Thieme Publications: New York, NY. January 2002.

Ernest Senz, **Matthew Ammerman**, Mark Grant, Damirez Fossett. "Chapter 38- Sciatic Nerve Exploration." Operative Neurosurgical Anatomy. Damirez Fossett MD and Anthony Caputy MD, Ed. Thieme Publications: New York, NY. January 2002.

Matthew Ammerman, Martin Baggenstos, Richard S Polin. "Back Pain." Medlink Neurology: www.medlink.com. 2005, 2006, 2007, 2008

Peer Reviewed Articles:

Whitney Helmes, Hyung Lee, **Matthew Ammerman**, Annette L. Parks, Marc A. T. Muskavitch, and Barry Yedvobnick. Engineered Truncations in the Drosophila Mastermind Protein Disrupt Notch Pathway Function. Developmental Biology. 215; p. 358-374,:1999.

Khalid MH, Shibata S, Furukawa K, Nadel A, **Ammerman MD**, Caputy AJ. Role of estrogen receptor-related antigen in initiating the growth of human glioma cells. J Neurosurg. 2004 May;100(5):923-30.

Richard S. Polin,, Nicholas F. Marko, **Matthew D Ammerman**, Mark E. Shaffrey, Wei Huang, Frederick A. Anderson Jr, Anthony J. Caputy, and Edward Laws. Functional outcome and survival in patients with high-grade gliomas in dominant and nondominant hemispheres. J Neurosurg 2005 Feb;102(2):276-83.

Ammerman JM, **Ammerman MD**, Dambrosia J, Ammerman BJ. A prospective evaluation of the role of intraoperative x-ray in lumbar discectomy. Predictors of the incorrect level exposure. Surg Neurol 2006 Nov:66(5):470-3.

Ammerman JM, **Ammerman MD**, Magram G. Subarachnoid air mimicking a basilar apex aneurysm. Case illustration. J Neurosurg Peds 2007 Mar:106(3) 244.

Ammerman JM, **Ammerman MD**, Leiphart JW. Traumatic bilateral thoracic facet dislocation without fracture. J American College of Surgeons 2008 Jan: 206(1) pp186-87.

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Ammerman JM, **Ammerman MD**. Wrong-sided surgery. J Neurosurg Spine 2008 Jul: 9(1) pp105-6.

Ammerman JM, Libricz J, **Ammerman MD**. The role of Osteocel Plus as a fusion substrate in minimally invasive instrument edtransforaminal lumbar interbody fusion. Clin Neurol Neurosurg. 2012 Nov: 12 pp531-8.

Posters:

Matthew Ammerman, Mark Grant, Ernest Senz, Juan Arzate, Amal Nadel, Anthony Caputy. Surgical Anantomy for Peripheral Nerve Surgey. Department of Neurological Surgery, George Washington University Medical Center, Washington, DC.

Mark Grant, **Matthew Ammerman,** H. Khalid, A. Nadel, D. Fossett, W. Weglicki, A. Caputy. Neuroprotection by Mg-Gluconate During Reperfusion in a Rat Model of Transient Focal Ischemia. Department of Neurological Surgery and Experiment Medicine. The George Washington University Medical Center, Washington, DC. (Presented at AANS meeting in Toronto)

Denis J DiAngelo, PhD, B. Dhillon MSc, **M. Ammerman MD**, M. Campos-Benetiz MD, B. Kelly PhD. A Novel Shear Expulsion Protocol for Evaluating the Holding Strength of Cervical Disc Arthroplasty Devices. University of Tennessee Biomedical Engineering, Memphis TN. (Presented at CSRS meeting in Charlotte, NC 2010)

Presentations:

Matthew Ammerman. Is BMP worth the hype? Presented at George Washington University, Department of Neurosurgery, Grand Rounds, 1-4-2005.

Matthew Ammerman. Defining a role for radiosurgery in the treatment of spinal tumors. Presented at George Washington University, Department of Neurosurgery, Grand Rounds, 2-14-2006.

Matthew Ammerman. Endoscopic management of aqueductal stenosis. Presented at George Washington University , Department of Neurosurgery, Grand Rounds. 2-6-2007

Matthew Ammerman. Mangament of type 2 dens fractures. Presented at George Washington University, Department of Neurosurgery, Grand Rounds. 9-11-07

Matthew Ammerman. Circulatory arrest for giant basilar aneurysms. Presented atGeorge Washington University, Department of Neurosurgery, Grand Rounds. 4-8-08

Matthew Ammerman, Kevin Foley. The Anabolic Effect of Plasma-Mediated Ablation on the Intervertebral Disc: Stimulation of Proteoglycan and IL-8 Production. Presented

at Spine Arthroplasty Society, London England. Department of Neurosurgery University of Tennessee. 4-30-09.

Matthew Ammerman. Introduction to Neurosurgery: A primer for medical students. Presented at George Washington University Medical School. Neuroanatomy Lecture series. 10-26-2009, 10-25-2010. 10/2011, 10/2012, 10/2013

Committees:

Investigational Review Board - Chairman Sibley Memorial Hospital (Johns Hopkins Medicine), Washington DC. Member 2009-current

Infection Control and Prevention Meeting - Sibley Memorial Hospital, Washington DC. Member 2009-2012

Pharmacy and Therapeutics Committee - Sibley Memorial Hospital, Washington DC. Member 2012-current

Credential Committee - Sibley Memorial Hospital, Washington DC. Member 2012-current

Foundations:

Board of Directors - **So What Else.** One Preserve Parkway, Suite 150. Rockville, MD 20852. 301-279-6990. 2016 to current. Focus on providing out of school time education and creative programming to underserved youth; promote volunteerism in the community.

Board of Trustees (chief science officer)- **Joseph Robert Shaw Foundation.** 5117 52nd Street, NW. Washington, DC 20016. 2017 to current. Focus on treatment/research for hypoid-anoxic brain injury.